MEMORIAL HOSPITAL ISSUE

DELAWARE STATE MEDICAL JOURNAL

Official Organ of the Medical Society of Delaware

INCORPORATED 1789

VOLUME 30 APRIL, 1958 NUMBER 4

INTESTINAL POLYPS

Complete Contents on Page iv

ORAL

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References: (1) Greenblatt, R. B., & Clark, S. L.: M. Clin. North America, Philadelphia, W. B. Saunders Company (Mar.) 1957, p. 587. (2) Greenblatt, R. B.: *J. Clin. Endocrinol.* *16*:869, 1956. (3) Hertz, R.; Waite, J. H., & Thomas, L. B.: *Proc. Soc. Exper. Biol. & Med.* *91*:418, 1956.

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DELAWARE STATE MEDICAL JOURNAL

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Articles are accepted for publication on condition that they are contributed solely to this JOURNAL. Manuscripts must be typewritten, double spaced, with wide margins, and the original copy submitted. Photographs and drawing for illustrations must be carefully marked and show clearly what is intended.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index Medicus, Published by the American Medical Association, Chicago.

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All advertisements are received subject to the approval of the Committee on Publication of the Medical Society of Delaware. Advertising forms close the 15th of the preceding month.

Subscription price: $5.00 per annum, in advance. Single copies, 75 cents. Foreign countries: $5.00 per annum.

Entered as second-class matter June 28, 1929, at the Post Office at Wilmington, Delaware, under the Act of March 3, 1879. Editorial Office: 1618 N. Broom Street, Wilmington, Delaware. Business Office: 621 Delaware Avenue, Wilmington, Delaware. Issued monthly.

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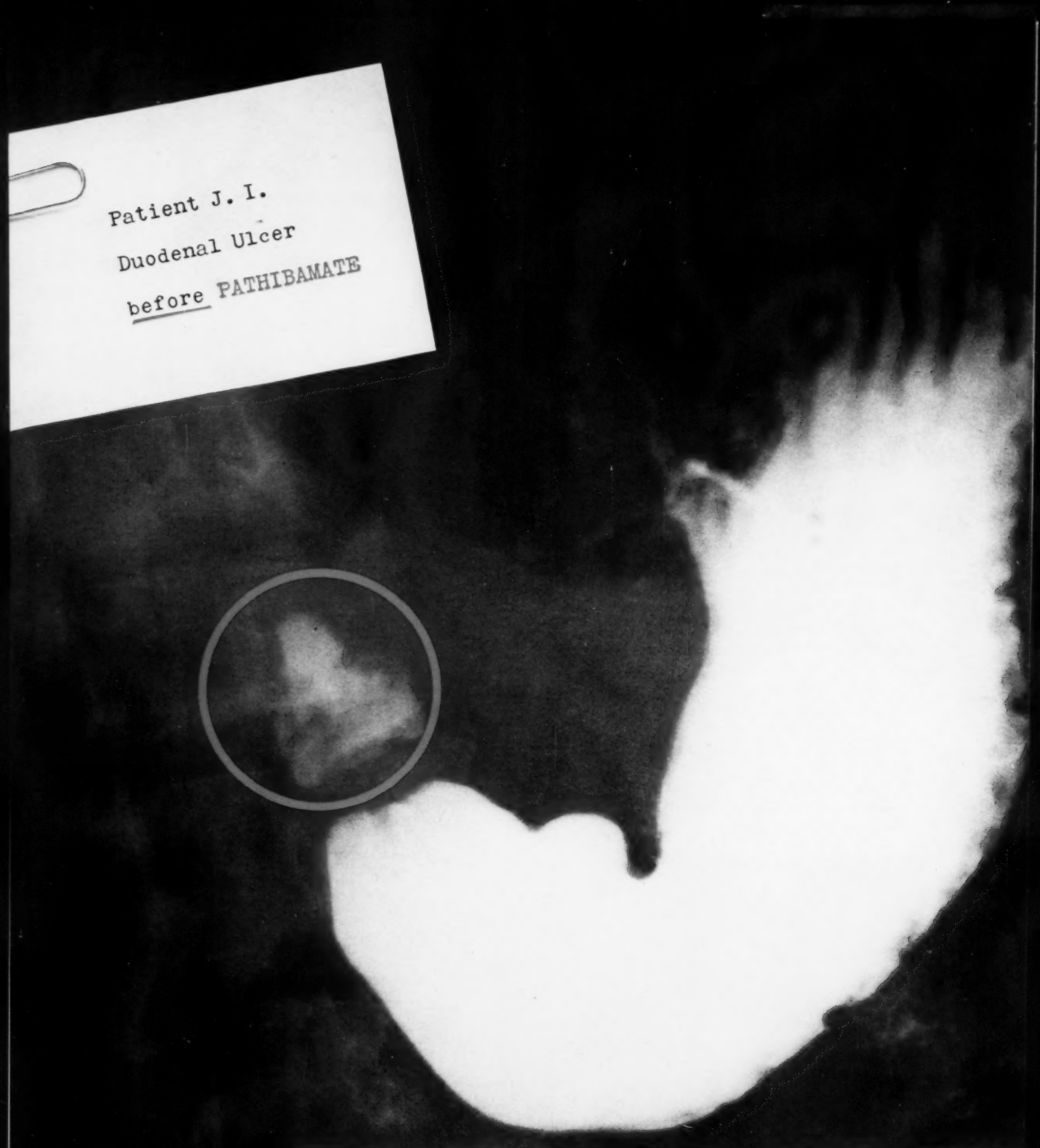

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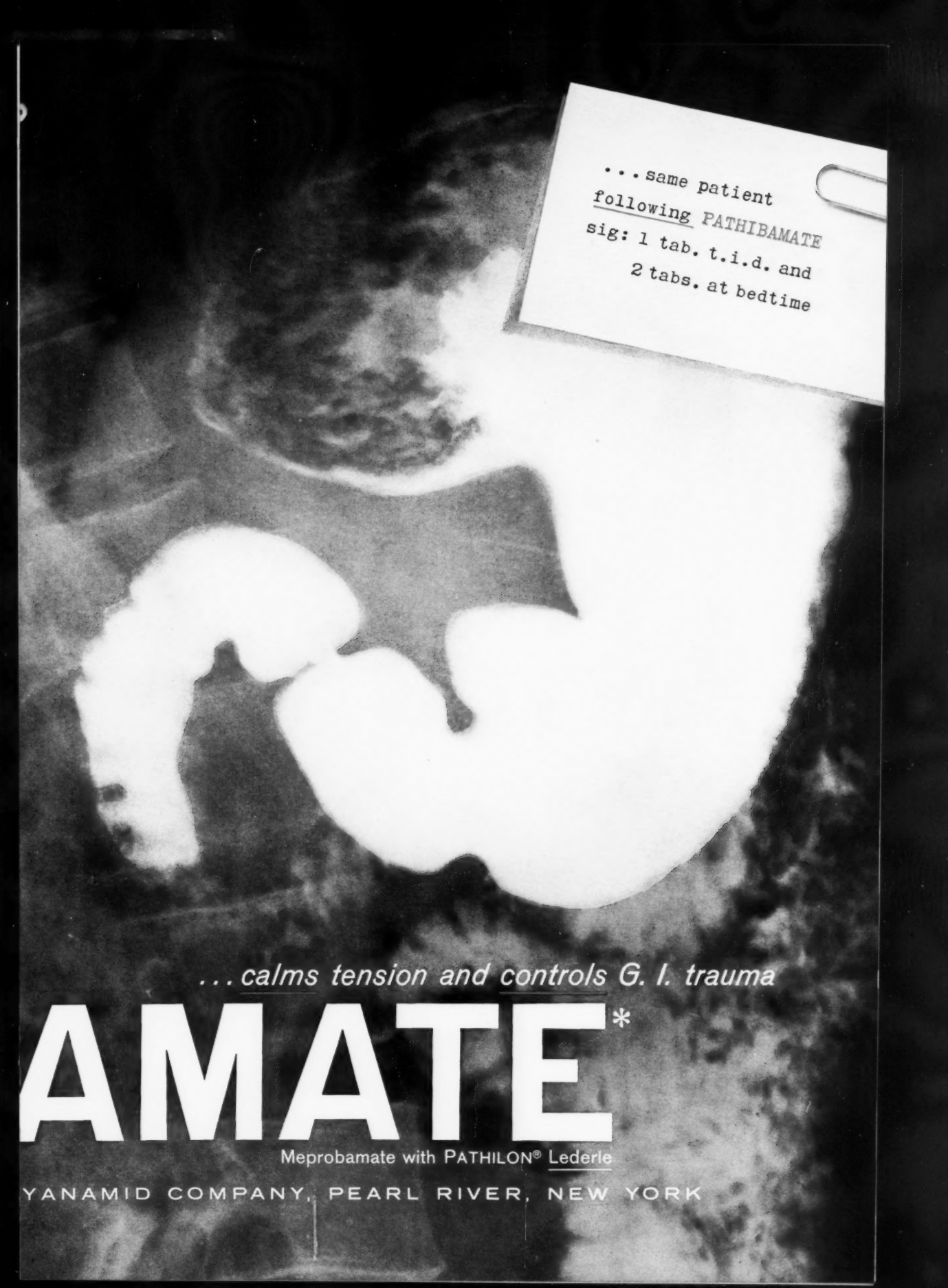
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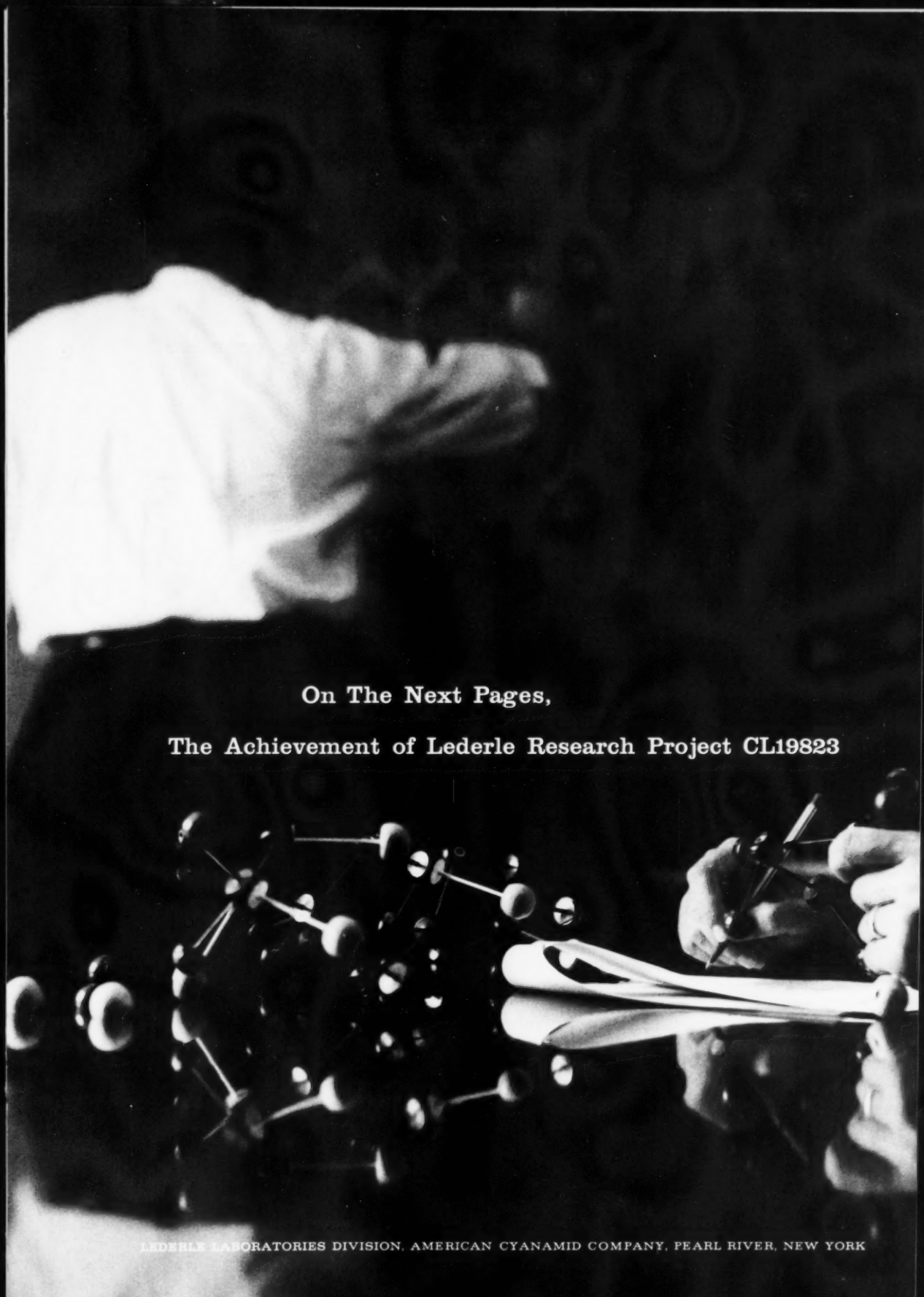
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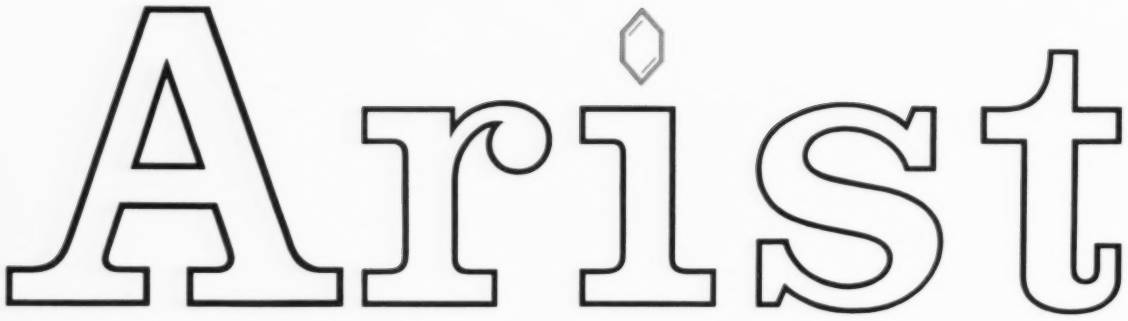

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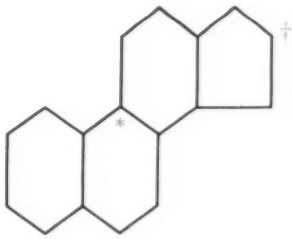

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Biological Effects of Aristocort

with

particular emphasis

on:

Kidney function

Animal studies on ARISTOCORT[1] have not demonstrated any interference with creatinine or urea clearance. Autopsy surveys of organs of animals on prolonged study of this medication have shown no renal damage.

Sodium and water

ARISTOCORT produced an increase of 230 per cent of water diuresis and 145 per cent sodium excretion when compared to control animals.[1] Metabolic balance studies in man revealed an average negative sodium balance of 0.8 Gm. per day throughout a 12-day period on a dosage of 30 mg. per day.[2] Additional balance studies showed actual sodium loss when ARISTOCORT was given in doses of 12 mg. daily.[3] Other investigators observed significant losses of sodium and water during balance studies and that those patients with edema from some older corticosteroids lost it when transferred to ARISTOCORT.[4,5] In two studies of various rheumatic disorders (194 cases) on prolonged treatment, sodium and water retention was not observed in a single case.[6,7]

Potassium and chlorides

There was no active excretion of potassium or chloride ions in animals given maintenance doses of ARISTOCORT 25 times that found to be clinically effective.[1] Potassium balance studies in humans[2,3] revealed that negative balance did not occur even with doses somewhat higher than those employed for prolonged therapy in rheumatoid arthritis. Hypokalemia, hyperkalemia or hypochloremia did not occur, when tested, in 194 patients with rheumatoid arthritis treated for up to ten and one-half months.[6,7]

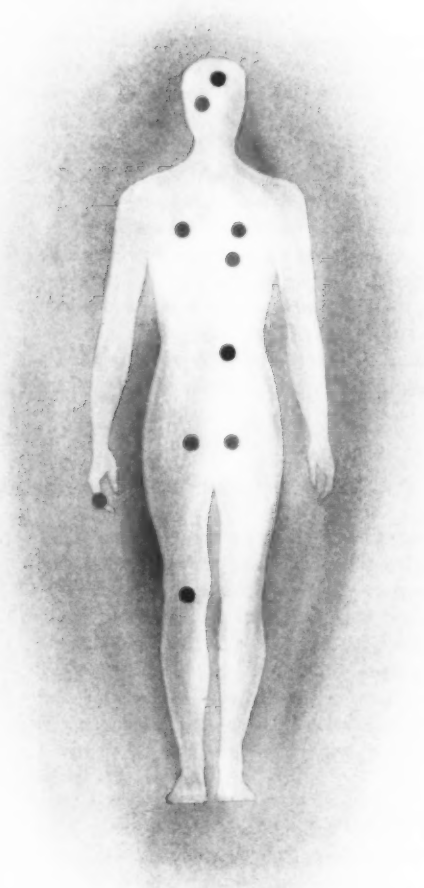
Calcium and phosphorus

Phosphate excretion in animals[1] was not changed from normal even with amounts 25 times greater (by body weight) than those known to be clinically effective. Human metabolic balance studies[3] demonstrated that no change in calcium excretion occurred on dosages usually employed clinically when the compound is administered for its anti-inflammatory effect. Even at a dosage level twice this, slight negative balance appeared only during a short period.

Protein and nitrogen balance

Positive nitrogen balance was maintained during a human metabolic study on maintenance dosage of 12 mg. per day.[3] At dosages two to three times normal levels, positive balance was maintained except for occasional short periods in metabolic studies of several weeks' duration.[2,3]

There was always a tendency for normalization of the A/G ratio and elevation of blood albumin when ARISTOCORT was used in treating the nephrotic syndrome.[8]



Liver glycogen deposition and inflammatory processes

An intimate correlation exists between the ability of a corticosteroid to cause deposition of glycogen in the liver and its capacity to ameliorate inflammatory processes.

In animal liver glycogen studies, relative potencies of ARISTOCORT over cortisone of up to 40 to 1 have been observed. Compared to ARISTOCORT, five to 12 times the amount of prednisone is required to produce varying but equal amounts of glycogen deposition in the liver.[1]

Most patients show normal fasting blood sugars on ARISTOCORT. Diabetic patients on ARISTOCORT may require increased insulin dosage, and occasional latent diabetics may develop the overt disease.

Anti-inflammatory potency of ARISTOCORT was determined by both the asbestos pellet[1] and cottonball[9] tests. It was found to be nine to 10 times more effective than hydrocortisone in this respect.

Gastric acidity and pepsin

The precise mode of ulcerogenesis during treatment with corticosteroids is not known. There is much experimental evidence for believing this may be related to the tendency of these agents to increase gastric pepsin and acidity—and this cannot be abolished by vagotomy, anticholinergic drugs or gastric antral resection.[10] Clinical studies[11] of patients on ARISTOCORT revealed that uropepsin excretion is not elevated. Further, their basal acidity and gastric response to histamine stimulation were within normal limits.

Central nervous system

The tendency of corticosteroids to produce euphoria, nervousness, mental instability, occasional convulsions and psychosis is well known.[12] The mechanism underlying these disturbances is not well understood.

ARISTOCORT, on the contrary, does not produce a false sense of well being, insomnia or tension except in rare instances. In the treatment of 824 patients, for up to one year, not a single case of psychosis has been produced. In general, it appears to maintain psychic equilibrium without producing cerebral stimulation or depression.

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Lederle

The Promise of Aristocort in Reduction of Side Effects

It is axiomatic to affirm that the undesirable collateral hormone effects of corticosteroids increase in frequency and severity the higher the dosage and the longer used.

It has also become well recognized that the most serious of the major side effects from long-term corticosteroid treatment are peptic ulcers, osteoporosis with fracture, drug psychosis and euphoria, and sodium and water retention leading often to general tissue edema and hypertension.

It is significant that of the close to 400 patients on the lower dosage schedules found effective in bronchial asthma and dermatologic conditions, only 1 case of peptic ulceration has developed. No other of the above side effects have been observed even though ARISTOCORT was administered continuously to them for periods as long as one year.

The treatment of rheumatoid arthritis with steroids appears to result in the highest incidence of side effects. For this reason, the side effects associated with ARISTOCORT therapy in 292 patients with rheumatoid arthritis are reported below.

Peptic Ulcer

The occurrence of peptic ulcer in 292 patients with rheumatoid arthritis treated continuously for up to one year with ARISTOCORT is approximately 1 per cent (2 of the 3 occurred in patients transferred from prednisone). In the remaining 532 cases recently analyzed, only one ulcer has been discovered in a patient who apparently had no ulcer when he was changed from another steroid.

Osteoporosis and Compression Fractures

The occurrence of osteoporosis with compression fracture in 292 patients with rheumatoid arthritis treated continuously for up to one year with ARISTOCORT is 0.33 per cent (1 case[1]). Although these results are encouraging, determination of the true incidence of osteoporosis will have to await the passage of more time.

Euphoria and Psychosis

The euphoria so commonly produced by all previous corticosteroids has seemed a most desirable attribute to patients. In penalty, however, they have often later to pay for this by mental disturbances, varying from mild and transitory to severe depression and psychosis,[2] and toxic syndromes producing even convulsions and death.[3]

Since the onset of these complications is not directly related to duration of steroid administration,[4] the fact that not one case of psychosis occurred in 824 patients treated with ARISTOCORT, is most encouraging.

Sodium Retention—Hypertension—Potassium Depletion

When 17 patients were changed from prednisone to ARISTOCORT, 11 rapidly lost weight although only one had had visible edema.[5] Sodium and water retention, hypokalemia or hyperkalemia and steroid hypertension did not appear in 194 rheumatoid arthritis patients treated with ARISTOCORT.[1,6]

The interrelation between blood and body sodium, and steroid hypertension has long been generally appreciated.[7,8] Except in rare instances, or when unusually high doses are used (e.g., leukemia), the problem of edema and hypertension caused by sodium and water retention, has been eliminated with ARISTOCORT.

Minor Side Effects

Collateral hormonal effects of less serious consequence occurred with approximately the same frequency as with the older corticosteroids.[1] These include erythema, easy bruising, acne, hypertrichosis, hot flashes and vertigo. Several investigators have reported symptoms not previously described as occurring with corticosteroid therapy, e.g., headaches, lightheadedness, tiredness, sleepiness and occasional weakness.

Moon facies and buffalo humping have been seen in some patients on ARISTOCORT. However, ARISTOCORT therapy, in many instances, resulted in diminution of "Cushingoid" signs induced by prior therapy. Where this occurs, it may be related to reduced dosage on which patients can be maintained.

Reduction of dosage by one-third to one-half

In a double-blind study of comparative dosage in patients with rheumatoid arthritis,[9] 70 per cent of the cases were as well controlled on a dose of ARISTOCORT one-half that of prednisone. A general recommendation can be made that ARISTOCORT be used in doses two-thirds that of prednisone or prednisolone in the treatment of rheumatoid arthritis. There are individual variations, however, and each patient should be carefully titrated to produce the desired amount of disease suppression.

Comparative studies, of patients changed from prednisone, indicate reduced dosage of ARISTOCORT in bronchial asthma and allergic rhinitis (33 per cent),[5] and in inflammatory and allergic skin diseases (33-50 per cent).[10,11]

General Precautions and Contraindications

Administration of ARISTOCORT has resulted in lower incidence of major serious side effects, and in fewer of the troublesome minor side effects known to occur with all previously available corticosteroids. However, since it is a highly potent glucocorticoid, with profound metabolic effects, all traditional contraindications to corticosteroid therapy should be observed.

No precautions are necessary in regard to dietary restriction of sodium or supplementation with potassium.

Since ARISTOCORT has less of the traditional side effects, the appearance of sodium and water retention, potassium depletion, or steroid hypertension cannot be used as signs of overdosage. As a rule patients will lose some weight during the first few days of treatment as a result of urinary output, but then the weight levels off.

Patients do not develop the abnormally voracious appetite common to previous corticosteroid administration. In fact, some patients experienced anorexia, and it is advisable to inform patients of this and to recommend they maintain a normal intake of food, with emphasis on liberal protein intake.

While precipitation of diabetes, peptic ulcer, osteoporosis, and psychosis can be expected to appear rarely from ARISTOCORT, they must be searched for periodically in patients on long-term steroid therapy.

Traditional precautions should be observed in gradually discontinuing therapy, in meeting the increased stress of operation, injury and shock, and in the development of intercurrent infection.

There is one overriding principle to be observed in the treatment of any disease with ARISTOCORT. *The amount of the drug used should be carefully titrated to find the smallest possible dose which will suppress symptoms.*

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Lederle

The Promise of Aristocort in Rheumatoid Arthritis

◇ ARISTOCORT *therapy has been intensely and extensively studied for periods up to one year on 292 patients with rheumatoid arthritis.*

Significant is the fact that most patients were *severe* arthritics, transferred to ARISTOCORT from other corticosteroids because satisfactory remission had not been attained, or because the seriousness of collateral hormonal effects had made discontinuance desirable.

Results of treatment

Freyberg and associates[1] treated 89 patients with rheumatoid arthritis (A. R. A. Class II or III and Stage II or III). Of these, 51 were on ARISTOCORT therapy from three to over 10 months. In all but a few patients, satisfactory suppression of rheumatoid activity was obtained with 10 mg. per day. Thirteen were controlled on 6 mg. or less a day, and for periods to 180 days. The investigators reported therapeutic effect in most cases to be A. R. A. Grade II (impressive) and that marked reduction in sedimentation rates occurred.

Another interesting observation in this study: Of the 89 patients treated, 12 had active ulcers, developed from prior steroid therapy. *In six patients, the ulcers healed while on doses of* ARISTOCORT *sufficient to control arthritic symptoms.*

Hartung[2] treated 67 cases of rheumatoid arthritis for up to 10 months. He found the optimum maintenance dose to be 11 mg. per day. Nineteen of these patients were treated for six to 10 months with an "excellent" therapeutic response.

Dosage and course of therapy

The initial dosage range recommended is 14 to 20 mg. per day—depending on the severity and acuteness of signs and symptoms. Dosage is divided into four parts and given with meals and at bedtime. Anti-rheumatic effect may be evident as early as eight hours, and full response often obtained within 24 hours. This dosage schedule should be continued for two or three days, or until all acute manifestations of the disease have subsided, whichever is later.

The maintenance level is arrived at by reduction of the total daily dosage in decrements of 2 mg. every three days. The range of maintenance therapy has been found to be from 2 mg. to 15 mg. per day—with only a very occasional patient requiring as much as 20 mg. per day. Patients requiring more than this should not be long continued on steroid therapy.

The aim of corticosteroid therapy in rheumatoid arthritis is to suppress the disease only to the stage which will enable the patient to carry out the required activities of normal living or to obtain reasonable comfort. The maintenance dose of ARISTOCORT to achieve this end is arrived at while making full use of all other established methods of controlling the disease.

ARISTOCORT is available in 2 mg. scored tablets (pink); 4 mg. scored tablets (white). Bottles of 30.

Bibliography

1. Freyberg, R. H., Berntsen, C. A., and Hellman, L.: Paper presented at International Congress on Rheumatic Diseases, Toronto, June 25, 1957. 2. Hartung, E. F.: Paper presented at Florida Academy of General Practice, St. Petersburg, Florida, Nov. 2, 1957.

Lederle

The Promise of Aristocort in Respiratory Allergies

About 200 patients with respiratory allergies have been treated with ARISTOCORT *for continuous periods up to eight months.*

Results of treatment

Sherwood and Cooke[1,2] gave ARISTOCORT to 42 patients with bronchial asthma and allergic rhinitis. Average dose needed to control the asthmatic group was approximately 6 mg. per day (range, 2 to 14 mg.). Results, which were called "good to excellent" in all but four, were achieved on one-third less than similarly effective doses of prednisone or prednisolone.

The investigators noted other major improvements in ARISTOCORT therapy over the older steroids. There was no increase in blood pressure in any patient: *on the contrary, in 12 patients, there was reduction of pressure when they were transferred to* ARISTOCORT. One patient had required auxiliary antihypertensive drug therapy; over a nine-week period on ARISTOCORT, the pressure gradually fell from 206/100 to 136/79. In another case, the pressure slowly dropped from 205/105 to 154/86.

The number of cases in which these investigators tried ARISTOCORT in allergic rhinitis was not large enough to provide significant averages. However, the range of effective therapy was from 2 to 6 mg. per day. These strikingly low daily doses resulted in control of all signs and symptoms.

Schwartz[3] treated 30 patients with chronic, intractable bronchial asthma. At an average daily dose of 7 mg., he reported "good to excellent" results in all but one. Spies,[4] Barach[5] and Segal,[6] reported similar results at average daily maintenance doses of 4 to 10 mg. of ARISTOCORT.

Dosage and course of therapy

The initial dosage range recommended is 8 to 14 mg. of ARISTOCORT daily. Although a rare, very severe case may require more than this on the first day of therapy, these dosages will usually result in prompt alleviation of dyspnea, wheezing and cyanosis. Patients are soon able to carry out a normal span of daily activity.

The maintenance level is arrived at by reduction of the total daily dose every three days in decrements of 2 mg.; in the over-all series, the average daily dose for bronchial asthma is approximately 8 to 10 mg. and for allergic rhinitis, 2 to 6 mg. per day. All total daily doses should be divided into four parts and given with meals and at bedtime. As in every condition where corticosteroids are employed, each patient's treatment should be individualized and the maintenance arrived at by careful titration against signs and symptoms of disease.

Patients with chronic bronchial asthma may require steroid therapy for several months. And since asthma may be associated with cardiac disease, especially in the older age groups, ARISTOCORT is particularly useful because of its ability to cause excretion of sodium and water.

ARISTOCORT is available in 2 mg. scored tablets (pink); 4 mg. scored tablets (white). Bottles of 30.

Bibliography

1. Sherwood, H., and Cooke, R. A.: J. Allergy 28:97, 1957. 2. Sherwood, H., and Cooke, R. A.: Personal Communication. 3. Schwartz, E.: Personal Communication. 4. Spies, T. D.: Personal Communication. 5. Barach, A. L.: Personal Communication. 6. Segal, M. S.: Personal Communication.

Lederle

The Promise of Aristocort

in Nephrotic Syndrome

Fourteen patients with the nephrotic syndrome have been treated with ARISTOCORT *for continuous periods of up to six weeks.*

Results of treatment

Hellman and associates[1,2] noted that ARISTOCORT, because of its favorable electrolyte effects, may well be the most desirable steroid to date in treatment of the nephrotic syndrome. However, thus far its use has been reported in only 14 children, of whom 8 had a complete diuresis and disappearance of all abnormal chemical findings. Four of the patients had diuresis, but continued to show some abnormal chemical findings, while two patients with signs of chronic renal disease failed to respond.

Dosage and course of therapy

In order to produce maximal response, 20 mg. should be given daily until diuresis occurs. The dose should then be decreased gradually and maintained around 10 mg. a day. After the patient has been in remission for some time, it may be advisable to diminish the dose gradually and discontinue ARISTOCORT.

in Pulmonary Emphysema and Fibrosis

Eleven patients with pulmonary emphysema and/or fibrosis were treated with ARISTOCORT *for continuous periods of over two months.*

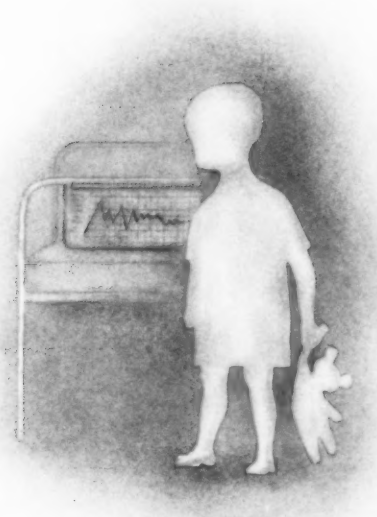
Results of treatment

Only small series of cases observed by Barach,[3] Segal,[4] and Cooke,[5] are available. Barach treated patients who were not adequately controlled by prednisone, with the same dose of ARISTOCORT with significant improvement.

Dosage and course of therapy

The initial suppressive dose range recommended is 10-14 mg. daily. Frequently, there is a prompt decrease in cyanosis and dyspnea, with increase in vital capacity.

The average maintenance dose level was 8 mg. a day. If it is desired to maintain a patient on continuous therapy for some months, dosages as low as 2 mg. a day have been successful. All decreases in dosage should be gradual and at a rate of 2 mg. decrements in total daily amount, every two to four days. The daily dosage is divided into four parts and given with meals and at bedtime.



in Neoplastic Diseases

Forty-four children and adults have been given ARISTOCORT *for palliative treatment of acute leukemia, chronic lymphatic leukemia, lymphosarcoma, lympholeukosarcoma and Hodgkin's disease.*

Results of treatment

Farber[6] has treated 22 children with acute leukemia for an average of three weeks. Of the 17 observed long enough to judge the efficacy of the medication, he rated five as excellent, three as good, two as fair and seven as poor responses.

Hellman and associates[7] gave ARISTOCORT to a group of patients with the various lymphomas in doses of 40 to 50 mg. a day—occasionally up to 100 milligrams. Treatment was continued in some cases for 17 weeks. Response was classified as good for the palliative purposes for which the drug was given.

Dosage and course of therapy

Massive initial suppressive doses of 40 to 50 mg. per day in children (1 mg./kg./day) and up to 100 mg. a day in adults have been administered.

Responses to any specific dosage in these conditions vary so widely that only a general dosage range can be indicated. Treatment must be individualized; rate of reduction in dosage and determination of maintenance levels cannot be categorized.

Miscellaneous

Patients with various other diseases have been treated by several clinical investigators. These include patients with osteoarthritis, acute bursitis, rheumatic fever, spondylitis, other "collagen-vascular" diseases (dermatomyositis, etc.), thrombocytopenic purpura, chronic eosinophilia, hemolytic anemia, diuretic-resistant congestive heart failures, and adrenogenital syndrome.

There have not been sufficient patients in any of the above categories to permit definitive treatment schedules to be finally established for ARISTOCORT. Additional studies are now in progress and physicians desiring information on any of these diseases are requested to write to Lederle Laboratories, Pearl River, New York for available data.

ARISTOCORT is available in 2 mg. scored tablets (pink); 4 mg. scored tablets (white). Bottles of 30.

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Lederle

The Promise of Aristocort

in Inflammatory and Allergic Skin Diseases

Over 200 patients with allergic and inflammatory skin diseases (including psoriasis, atopic dermatitis, exfoliative dermatitis, pemphigus, dermatitis herpetiformis, eczematoid dermatitis, contact dermatitis and angioneurotic edema) have been treated continuously with ARISTOCORT *for periods of up to eight months.*

Results of treatment

Rein and associates[1] treated 26 patients with severe dermatitis. Twenty-four had been on prednisone when changed to ARISTOCORT. While some had found satisfactory symptomatic relief, others had also developed side effects—moon face, buffalo hump, increased appetite with excessive weight increases and gastro-intestinal disturbances.

These investigators determined the equivalent dosage of ARISTOCORT to be approximately two-thirds that required to control symptoms on the previous corticosteroid. Thirteen of the 26, who had developed moon face, noted either an actual decrease or no further increase when transferred to ARISTOCORT. In addition: *Voracious appetites disappeared, with loss of weight in 11 patients; there was no elevation in blood pressure, and no necessity to restrict sodium or administer supplemental potassium.* Sherwood and Cooke,[2] and Shelley and Pillsbury[3] obtained similar results in allied disorders.

Hollander[4] first observed that ARISTOCORT appears to have striking affinity for the skin and great activity in controlling such diseases as psoriasis, for which other corticosteroids have been indifferently effective. Shelley and Pillsbury,[3] in 50 cases of acute extending psoriasis found that over 60 per cent were markedly improved.

Dosage and course of therapy

The recommended initial suppressive dose range is 14 to 20 mg. per day. In very severe cases, temporary dosages up to 32 mg. a day have been successfully employed. Once lesions are suppressed, gradually reduce dose to the maintenance level—which may be as low as 2 mg. per day.

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ARISTOCORT is available in 2 mg. scored tablets (pink); 4 mg. scored tablets (white). Bottles of 30.

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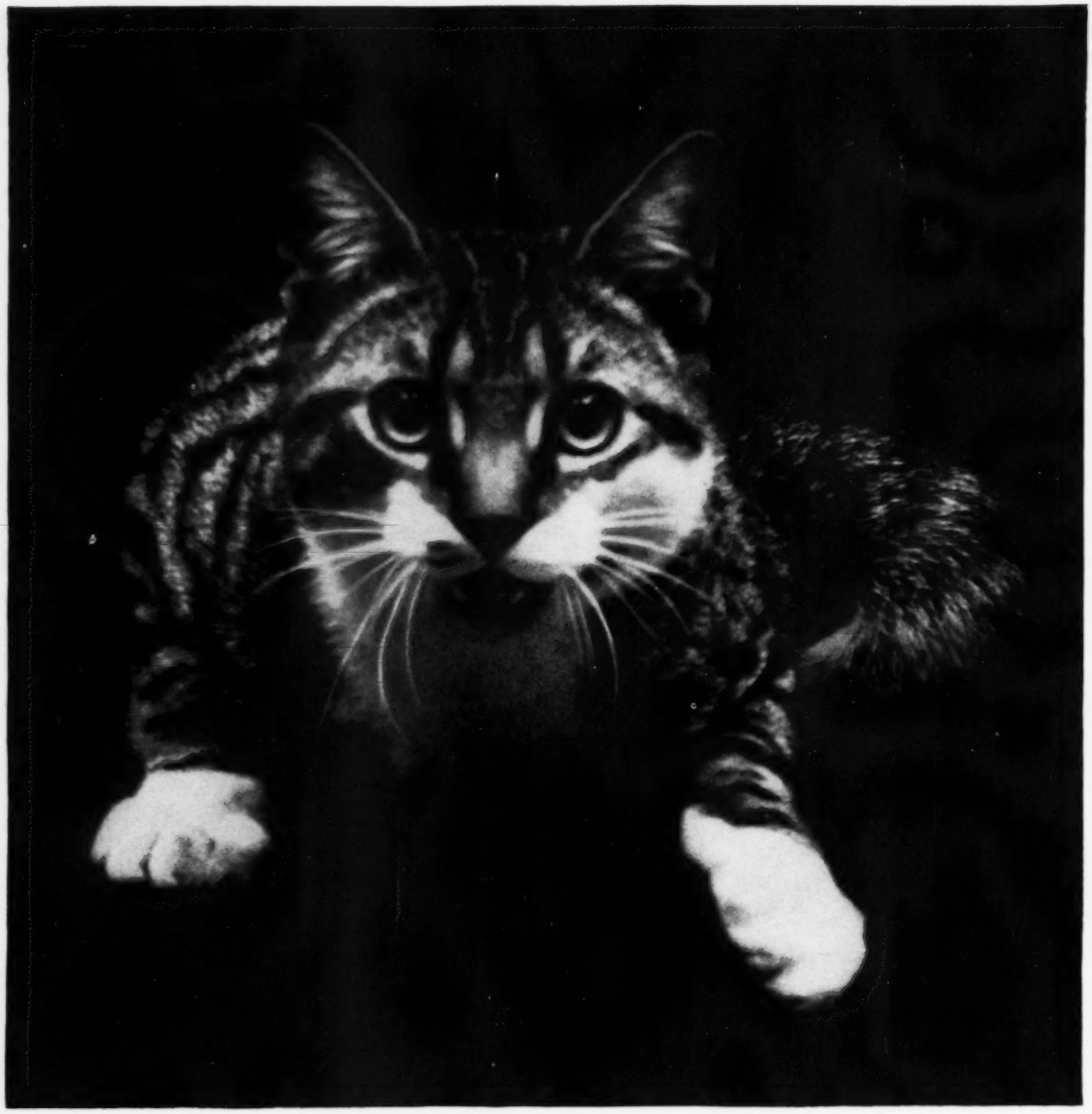
Lederle



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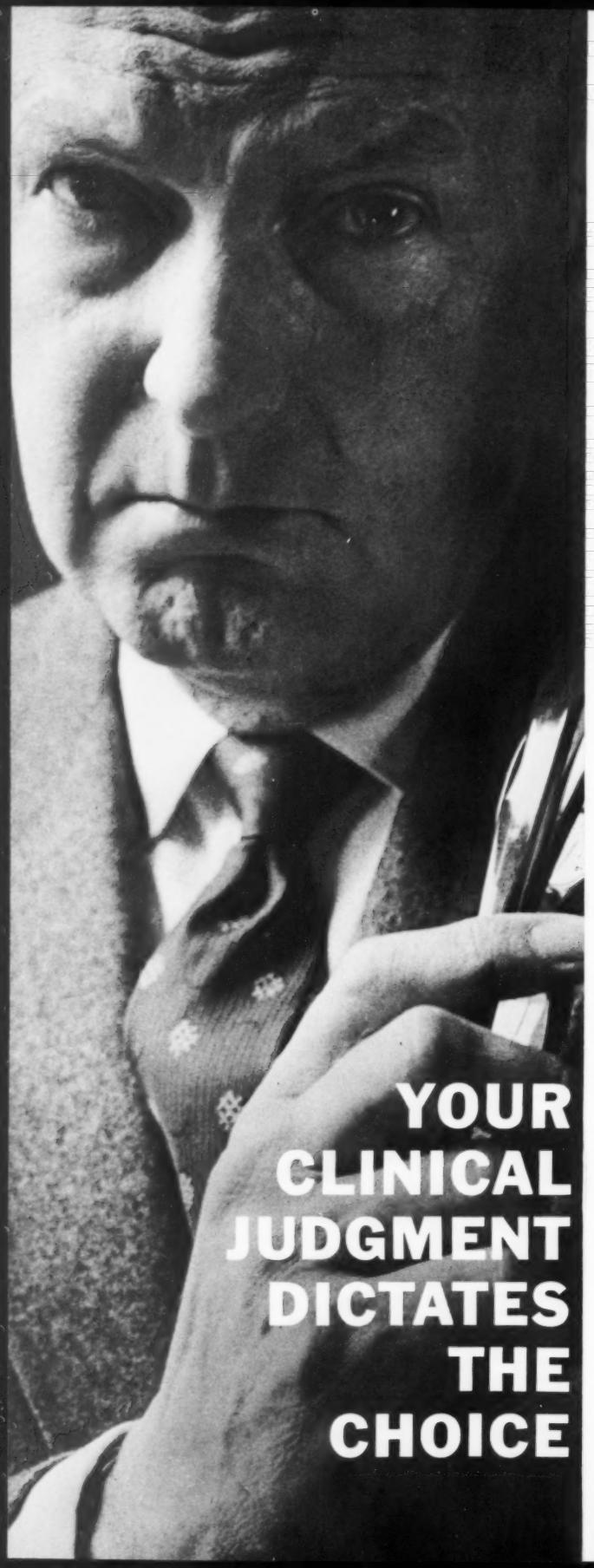

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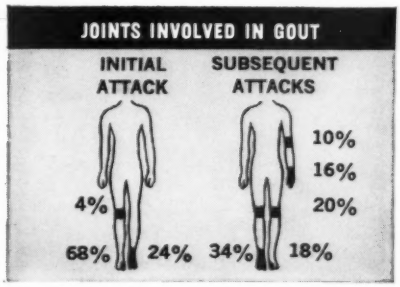

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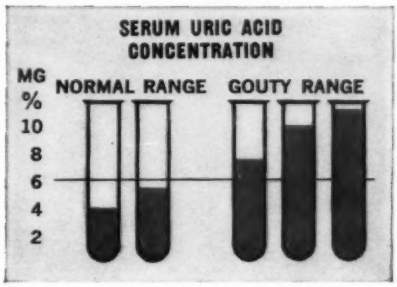

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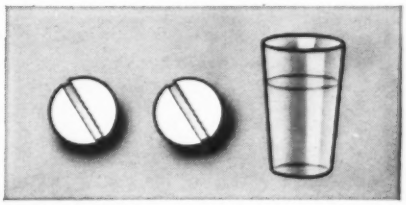

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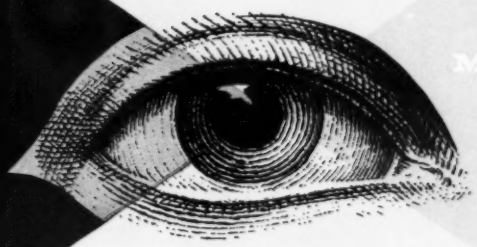

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Issued Monthly Under the Supervision of the Publication Committee
Owned and Published by the Medical Society of Delaware

VOLUME 30 APRIL, 1958 NUMBER 4

BENIGN AND MALIGNANT POLYPS OF LARGE INTESTINE

PATRICK F. ASHLEY, M.D.*

Although several excellent articles have appeared in the literature on the subject of benign and malignant intestinal polyps, there is still difficulty in interpreting the varied microscopic growth patterns and in deciding the correct type of surgical attack on these lesions. It is the purpose of this report to classify and describe the histologic types, to discuss the criteria for malignant change, and to see to what extent histopathologic changes influence choice of therapy. The word "polyp" is used in a restricted sense, limited to benign mucosal neoplasms, either sessile or pedunculated in type.

CLASSIFICATION

1. Adenomatous polyp (adenoma, adult adenoma)
2. Papillomatous polyp (papilloma, papillary adenoma, villous adenoma)
3. Juvenile polyp (retention polyp, adenoma of childhood)

MORPHOLOGY

Adenomatous polypy (Fig. 1). This variety is characteristically pedunculated and only a few are truly sessile. The smaller lesions are generally smooth and regular while the larger ones tend to be lobulated. Microscopically there is a mucosa-covered connective tissue core or stalk carrying with it, from the adjacent bowel wall, a muscularis mucosa and an extension, varying in length, of the submucosa with its attendant lymphatic and vascular channels. The covering mucosal epithelium is characterized by mature mucus secreting cells of the goblet type forming regular glands resembling those of normal colonic mucosa. Between the glands there is a variable quantity of connective tissue corresponding to the lamina propria of the colon.

Papillomatous polyp (Fig. 2). This variety is characteristically of large size, flat and sessile, with a papillary or finely lobular surface. Microscopically there are frond-like villous projections covered by tall columnar epithelial cells more often of the non-secreting type. Irregular shaped glands with frequent involutions are often present in the deeper portions. This variety of polyp presumably develops its characteristic appearance by arising from the surface epithelium (Fig. 3) as contrasted with the adenomatous variety which arises from the mucosal glands (Sunderland and Binkley[7]).

Juvenile polyp (Figs. 4 & 5). This type is pedunculated and regular in outline. Microscopically there is an abundant usually chronically inflamed stroma in which eosinophiles may predominate. The glands are sparse and frequently show cystic dilatation. The surface epithelium is usually replaced by granulation tissue.

ATYPICAL CHANGES IN BENIGN POLYPS

Frequently atypical changes are observed in benign polyps which are sometimes misinterpreted as carcinoma, whereas in reality the changes represent what is termed atypical hyperplasia. No apparent direct transition from atypical hyperplasia

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to carcinomatous change was noted by one group of writers who studied the problem.[7] These atypical changes include pseudostratification of cell nuclei, frequent mitoses, and loss of secretory activity with consequent deep straining of the epithelial cells (Fig. 6). Another misleading feature in pedunculated polyps, according to Fisher and Turnbull[2], is the apparent presence of glands beneath the muscularis mucosa. This finding, which might well be interpreted as invasion, is really an artifact due to a plane of section through a twisted pedicle.

CRITERIA FOR CARCINOMA ARISING IN BENIGN POLYPS

Swinton and Warren[8] suggested three important microscopic criteria for malignancy which are generally used by all writers in this field. These are:

1. *Anaplasia.* This is characterized by variation in the size and shape of cells and their nuclei, variation in chromatin content and arrangement, atypical mitoses, and prominent nucleoli.

2. *Irregularity of Architecture.* This is characterized by true epithelial stratification, intraglandular budding, and loss of cellular and nuclear polarity. The intraglandular proliferation of cells produces a gland-like structure and cell masses which are not separated by a limiting membrane.

3. *Invasion.* Invasion is recognized when no definite border is apparent between the epithelial cells and the surrounding stroma.

In order to make a definite diagnosis of malignancy at least two of the above three factors must be present. However, even when occurring alone, definite lymphatic or intravascular invasion nearly always means a malignant lesion.

Grossly, a polyp has no definite constant feature indicative of malignant change. Although ulceration and induration are noted features of malignant polyps, these changes may occur in benign lesions as a result of inflammation, fibrosis and hemorrhage.

CLASSIFICATION OF CARCINOMA ARISING IN POLYPS (After Fisher and Turnbull[2])

1. *Carcinoma-in-situ* (Fig. 7). This is characterized by anaplasia and irregularity limited to the glandular elements of the polyp without evidence of invasion.

2. *Superficial Carcinoma* (Fig. 8). This is characterized not only by the cellular atypia and irregularity described above but also reduplication of lumina and invasion of the lamina propria. There is no extension into the muscularis mucosa, lymphatic, or vascular spaces.

3. *Invasive Carcinoma* (Fig. 9). This reveals invasion of the muscularis mucosa and/or vascular and lymphatic channels. The differentiation of superficial carcinoma from the invasive type is simplified by the presence of a definite fibrous tumor stroma in the latter.

TREATMENT AND DISCUSSION

It is now widely accepted that the polyps under discussion are true neoplasms and should be removed. The extirpation of these polyps is dependent on a number of factors, chief amongst which are:

1. Type of polyp.
2. Natural history of the polyp.
3. Presence or absence of malignant change.
4. Possible multiplicity of lesions.
5. Age of patient.

Because of these factors it is necessary to discuss each type of polyp separately and a few generalizations are then possible with regard to surgical management.

Adenomatous polyp. The adenomatous polyp is by far the commonest variety reaching a maximum incidence of 24% in the eighth decade.[3] In nearly 50% of cases the polyps are scattered or multiple. This occurrence is often called multiple polyposis or adenomatosis coli but is to be sharply differentiated from the rare familial or congenital multiple polyposis in which condition malignant transformation is a

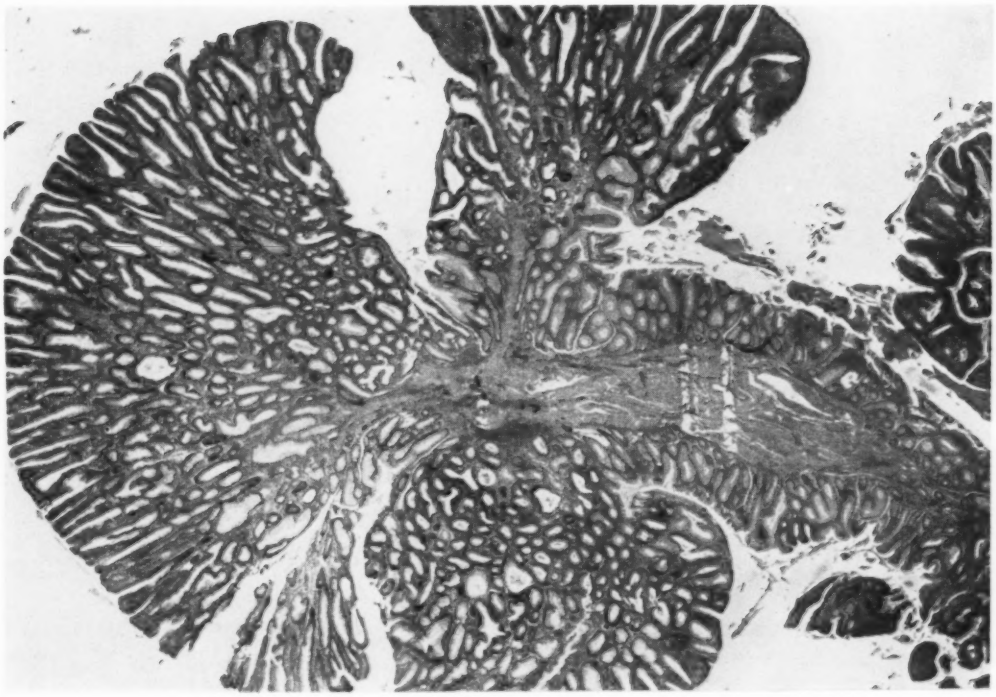

Figure 1
Adenomatous polyp, pedunculated. H & E x 25.

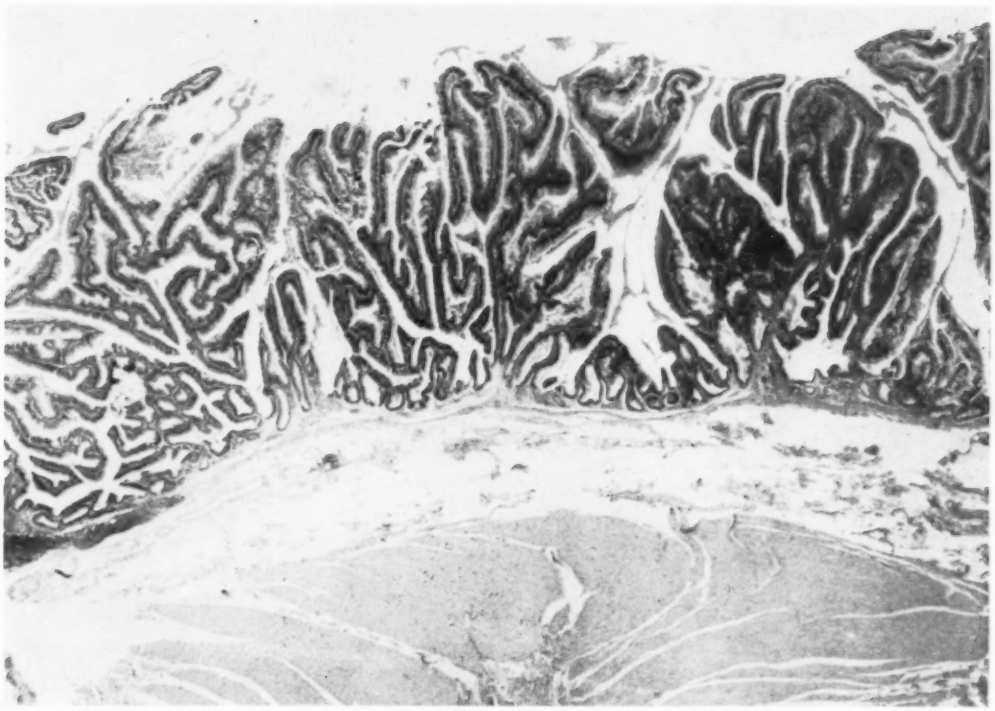

Figure 2
Papillomatous polyp, sessile. Note long thin villous projections. H & E x 25.

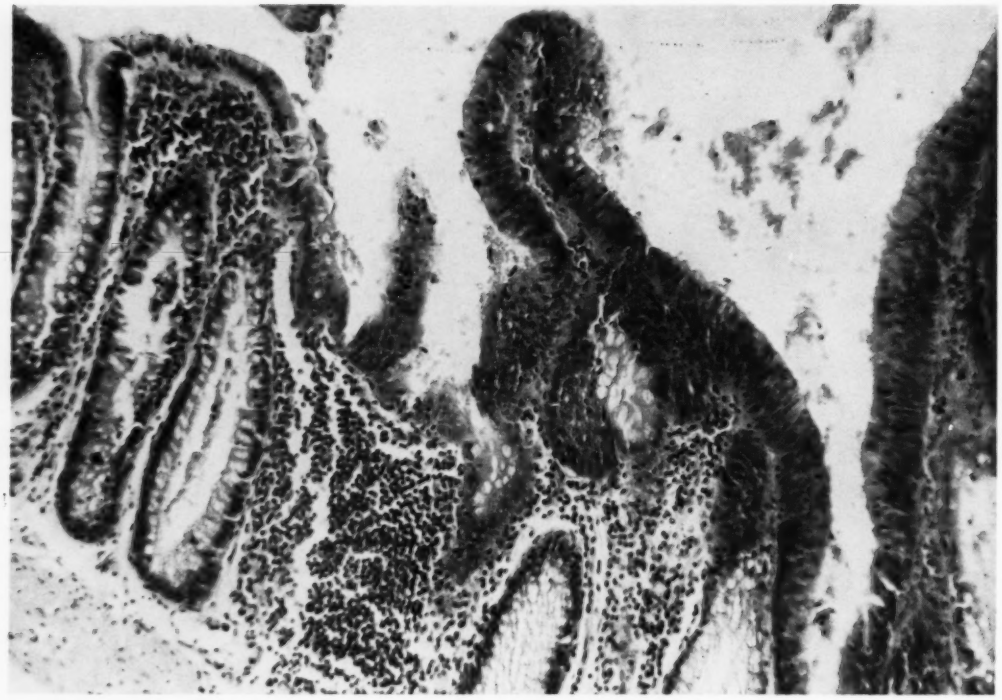

FIGURE 3
Papillomatous polyp. Note origin of villous process from surface epithelium. H & E x 120.

FIGURE 4
Juvenile polyp. Note large amount of stroma and cystic glands. H & E x 25.

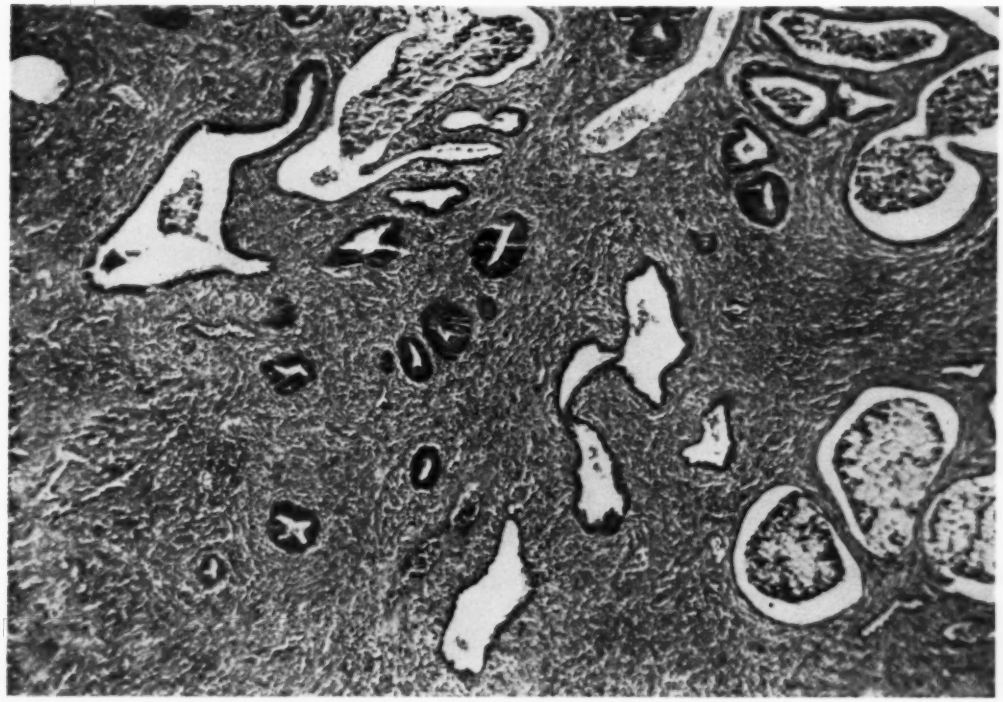

Figure 5
Juvenile polyp. Higher magnification of Figure 4. H & E x 75.

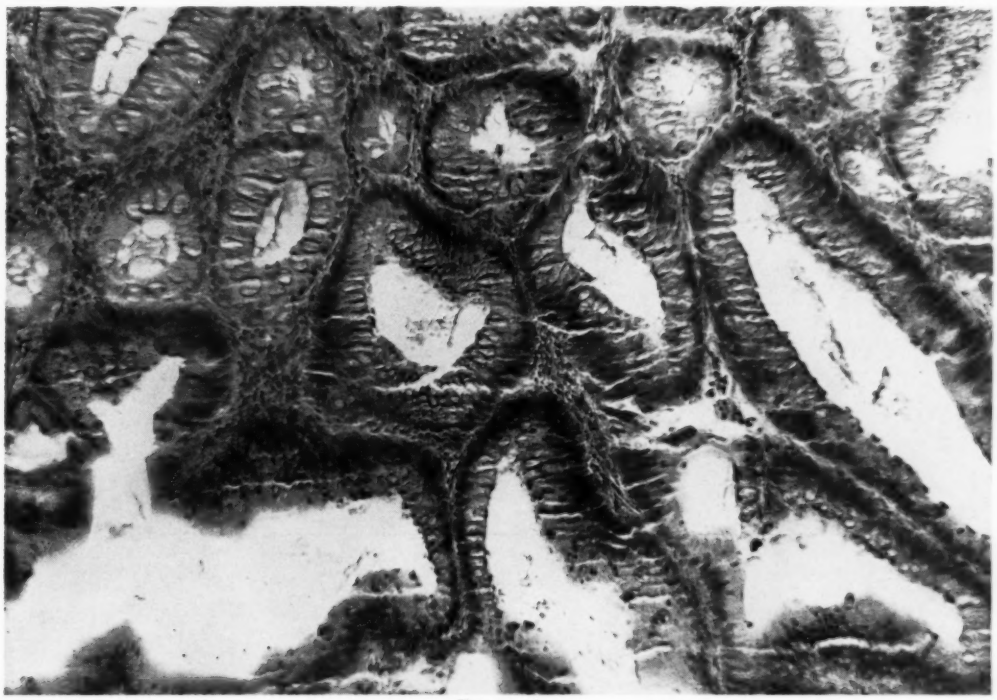

Figure 6
Atypical hyperplasia in adenomatous polyp. Note glands below showing irregularity in shape and deep staining cells. H & E x 120.

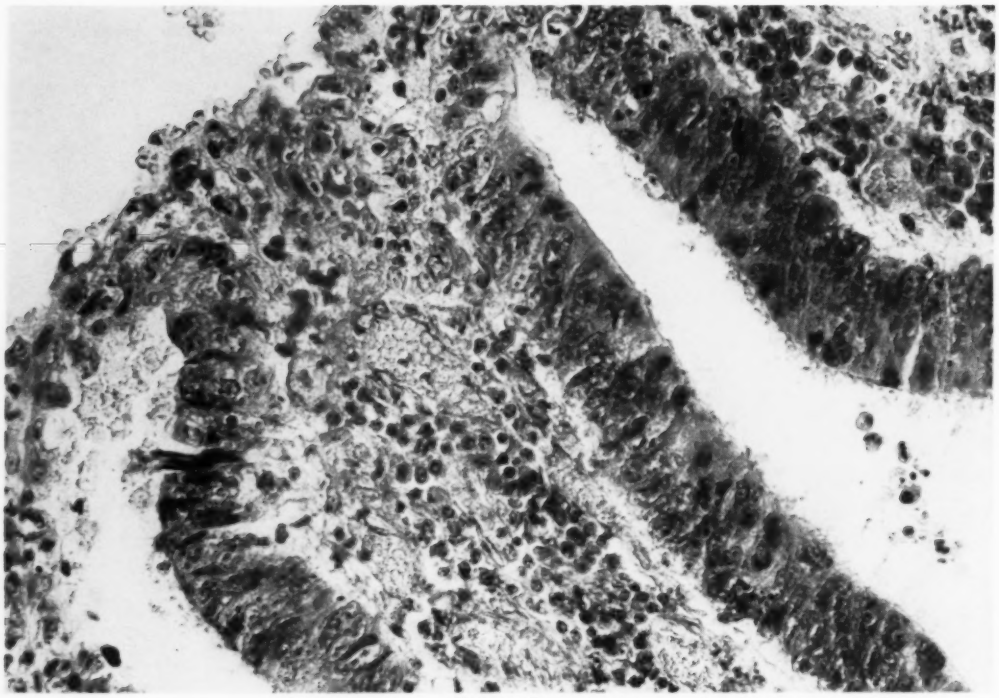

FIGURE 7
Carcinoma-in-situ in adenomatous polyp. Note nuclear atypism, stratification, loss of polarity and atypical mitoses. H & E x 400.

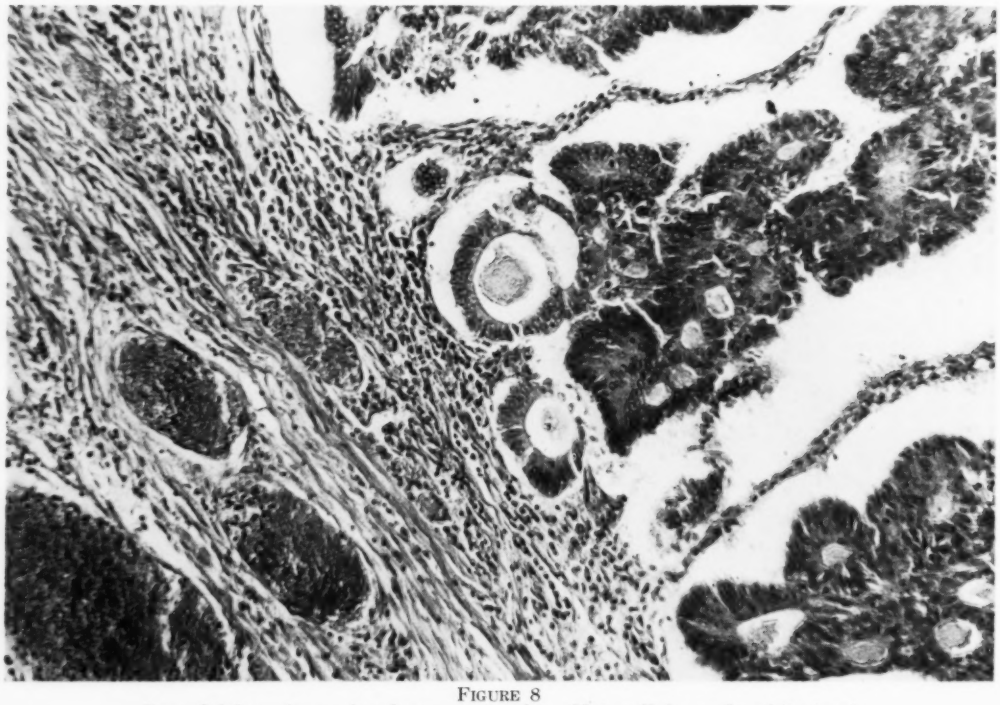

FIGURE 8
Superficial carcinoma in adenomatous polyp. Note cellular and architectural atypism. Muscularis mucosa and submucosa not invaded. H & E x 120.

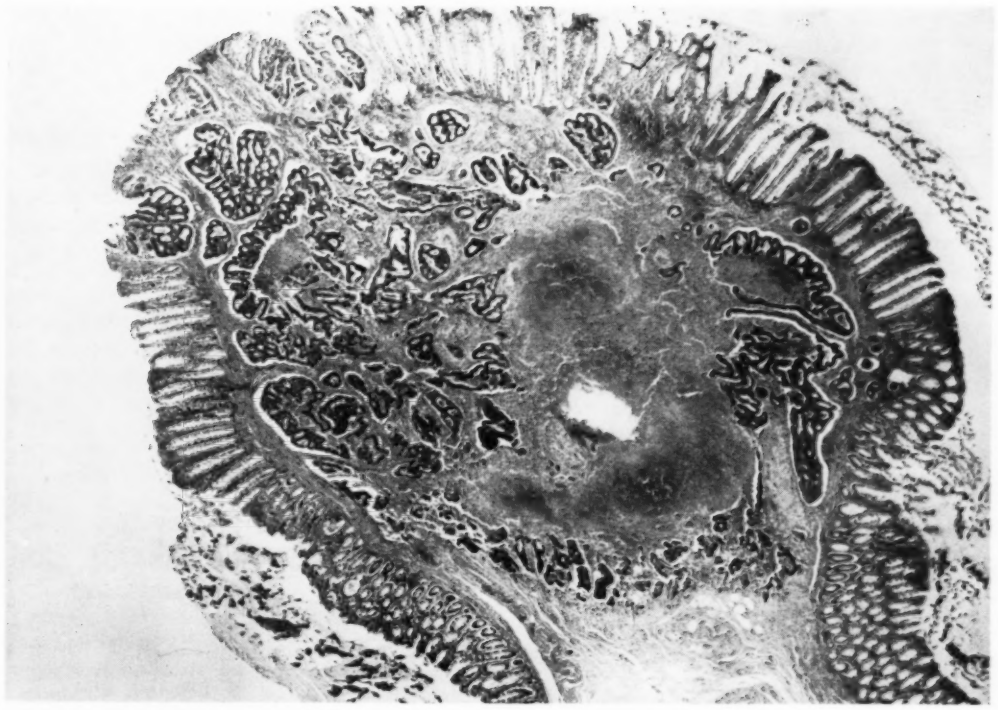

Figure 9
Invasive carcinoma in adenomatous polyp. Note extension into submucosa of stalk. H & E x 25.

certainty. Excluding this latter condition Helwig[3] found, in a series of autopsies, that 7.2% of colons having benign polyps also had one or more malignant polyps. Swinton and Warren[5] found malignancy occurring in approximately 14% of their series of polyps.

It has been shown that complete clinical cure of all benign adenomatous polyps and those showing carcinoma-in-situ or superficial carcinoma can be expected with local removal (with or without coagulation of the base) either through proctosigmoidoscopy or colotomy[1,2,6]. Polyps showing invasive carcinoma are apt to recur as frankly invasive colonic or rectal adenocarcinomas if treated locally[6]. Therefore, radical surgery with removal of a segment of bowel together with its lymphatic and vascular supply is indicative if invasive carcinoma is present in the stalk, base, or adjacent bowel wall.

Papillomatous polyp. In comparison with adenomatous polyps this variety is decidedly rare. They are usually solitary, confined predominantly to the rectum, and occur generally in the older age groups. Sunderland and Binkley[7] in a series of 48 cases found carcinoma-in-situ in nearly 70% and invasive carcinoma ultimately developed in nearly 40%. Local excision may suffice if the polyp is small and histologically benign but even then recurrence is prone to occur. Resection of the rectum appears indicated for the benign polyps that cannot be fully removed or controlled locally and for those polyps that show non-invasive carcinomatous transformation. Invasive carcinoma is prima facie evidence for resection for, due to its sessile nature, the submucosa is readily and directly invaded.

Juvenile polyp. Helwig[4] estimates that approximately 3% of children have juvenile polyps. This is exclusive of the first year of life during which period they are rare. Usually they are solitary with the sigmoid and rectum the site of predilection. It is

extremely doubtful if malignant change ever occurs in these lesions. As they are seldom encountered in adults, it is interesting to speculate on just what happens to them. Whereas some maintain they transform into the adult type (adenomatous polyp), the majority of investigators feel they become necrotic and slough. If the latter fate be true, our main concern in removal is for symptomatic relief and not for cancer prevention. Occasionally an adenomatous polyp is found in childhood and this requires investigation to rule out the possibility of congenital multiple polyposis.[5]

COMMENT

For the successful management of intestinal polyps there should be close cooperation between surgeon and pathologist. Adequate biopsies or preferably the entire polyp should be submitted for examination and multiple well oriented histologic preparations made. A diagnosis of "malignant polyp" is meaningless unless accompanied by a description of the type of polyp and the site and extent of malignant transformation. Grading of malignancy with respect to cellular anaplasia alone is also meaningless as the employment of conservative or radical surgery is largely based on the anatomic extent and not the grade of malignancy.

Frozen section may sometimes be of distinct value in the management of polyps removed at colotomy. If there is a focus of infiltrating carcinoma, the fibrous reaction produced permits suitable tissue for examination.

Finally, while generalizations with regard to therapy are possible, it must be emphasized that each case be individually studied and appropriate therapy applied after consideration of all pertinent factors.

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TRANSPLANTATION IN THE TREATMENT OF BURNS*

Leopold Scheiber, M.D.**

The surgical treatment of burns has been receiving increasing attention. Literature dealing with the therapy of burns indicates changes in theory as well as in practice.

Industrial development and expansion have been accompanied by an increase in the incidence of tissue damage from burns. Therapies and medical techniques have undergone great changes. Some patients with such injuries may now be treated in special hospital wards built or organized specifically for this purpose. Such advances should not be taken to imply that the treatment of burns has been perfected, or that all burns are treated best by the same method. Further improvements are needed.

The modern treatment of shock with parenteral fluids, including whole blood and plasma, together with antibiotics, supports the extensively burned patient so that a transplantation may be performed. Reverdin[1] and Thiersch[2] in the last century attempted transplantation, but the injured person died either from shock or infection before the operation could be completed.

Goldzieher and Makai[3] summarized the literature on transplantation published prior to 1912. Shortly therafter, in connection with accidental injuries, Kubanyi[4] began work on transplantation of the skin itself and the "laying of skin patches." The last 20 years has brought much progress in this field. Shock and infection can be successfully combated, and the skin needed for transplantation can be stored in freezing compartments of refrigerators. Stored transplantation pieces hold promise of more success than fresh tissue because through refrigeration the quantity of the individual "texture-antigen" (despecification of texture) decreases.[4a]

The absence of skin provides a portal of entry for pathogenic organisms and results in extensive, significant loss of fluids. Also, heat control is impaired. Therefore, the part of the body lacking epithelial tissue has to be covered with substitute tissues as soon as possible. For this transplantation, homotransplants, postmortem homografts, and either fresh or preserved amnion membrane can be used. Amnion can be obtained either from a Caesarean section or a normal delivery. Brown[5,6] points out that changes in the patient's general condition varies in direct proportion to the area of burned skin and emphasizes the significance of the postmortem homograft as a "biological dressing." He also proposed the use of amnion to cover burned parts of the body. Douglas[7,8] and others have demonstrated by means of animal experiments that the seronegative amnion, which remains viable longer than skin transplant, can be successfully used under aseptic conditions.

Kubanyi[9] accomplished the first application of amnion derived from a Caesarean section. A later attempt was made to preserve by refrigeration amnion obtained from normal birth. If refrigeration is prompt, the intra- and inter-cell liquid will freeze into small, thin crystals, so that the cell and tissue structure is not damaged or changed. The membrane is stored in a Duward bottle at 20-30°C. Before use, the amnion is heated in a sterile saline solution at 40°C. Grunfeld and Wenzl[10] maintain the amnion in identically grouped conserved blood. They stress that the derivation of the amnion can be other than a Caesarean section. The blood used for storage by Moser is maintained at an even temperature between 2 and 4°C. After it is four weeks old, the amnion originating from normal birth is strong enough to live.

* This work was performed at St. Rokus Hospital, Budapest, Hungary.

** Present address: Memorial Hospital, Wilmington.

Bacteriological examinations of amnion have revealed the presence of *Bacillus coli, Doderlein's bacillus,* and *hemolytic streptococcus.* This necessitated sterilization of the membrane by steam. Amnion which is conserved in blood, viable, and sterilized by steam has proved to be the tissue of choice for reasonable success as a transplant for covering peritoneal defects.

The amnion is placed on the defective skin part and may be sewn at the edges. A pressure bandage may also be used, but if the pressure is too great, an ischemic necrosis may occur.

Definitive success with homotransplantation can be expected only in the case of identical twins. In other cases, the skin graft will be repulsed earlier or later after temporary adherence. The greater the commonality between the glood group system of donor and that of the recipient, the longer will be the life of the skin graft. Because a homotransplantation is the combat of biological defense substance, an organ with an appreciable degree of homogenized antigen structure is desirable for overplanting. Such an organ is amnion.

Kubanyi used amnion for the first time in 1941 for covering skin defects which were not directly caused by burns. In 1943, he again used it in his first attempt at compensation for peritoneal defects. Since that time interest in the storage of amnion for covering of burns has heightened (independent from the Caesarean section of normal birth and that also the necessary examinations, Wasserman reaction, determination of blood groups, Rh-factor, does not have to be compared with all the time, as this can be done by refrigeration.)

Burns have recently been treated by homotransplantation, and covering with lyophilized skin has proved successful in more than a few reported cases. The organization of skin donors also has progressed. While skin parts from postmortems have not yet been used, attempts are being made to store skin taken from living human beings for use as grafts. The "skin-bank" mentioned in the literature is the depository for skin from neonatal deaths and adult victims of accidental death. The skin is removed with a dermatome and stored in fluid nitrogen at —79°C.

Sterling[11] in 1956 reported two cases in which the burnt skin was covered with amnion. One of the patients was a woman 38 years of age who sustained flame burns covering 60 per cent of her body. Five weeks after the accident occurred, amnion transplantation was attempted. Marked improvement followed transplantation, but the woman later died from a lung embolus. The other patient, a six-year-old boy, had flame burns covering 65 per cent of his body. Sterling covered the skin defects with amnion obtained from two Caesarean sections three weeks after the accident occurred. This patient recovered.

The author's[12] experience with the use of amnion and homotransplantation in this instance case may be of interest and significance. The amnion used by the author in 1952 for the covering of skin defects was unsuccessful. This same case was the first report in Hungary of successful use of homotransplantation for burns. (Frank[13])

On August 21, 1952, a girl, age 9, was transferred to *St. Rokus* hospital from another hospital where she had previously undergone conservative therapy for flame burns. The patient was emaciated and anemic. (Fig. 1). She had second degree burns extending over approximately 50 per

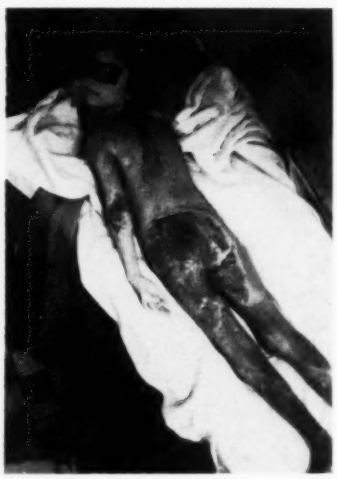

FIGURE 1
Patient showing second degree burns of buttocks, left leg and elbow.

cent of the body, on the buttocks, left leg, and left elbow. On August 28, 1952, fresh amnion derived from a Caesarean section was used to cover the skin defects. Injections of penicillin and saline solution dressings were used, but the body temperature increased from 100°F. to 102°F. Suppuration occurred, and the amnion had to be removed. The patient received penicillin, vitamins, and five blood transfusions (100 cc each). On September 10, 1952, "iso-agglutination-sampling" and corresponding preparations (blood group: B(111), Rh (D) +) by Reverdin from mother to daughter (syngenesia), a homotransplantation of skin from the mother's body to the left elbow, the left foot, and the buttocks of the patient (Figs. 2 and 3) was performed. Next, the limbs were placed in plaster casts. The patient's appetite and general condition improved. After two weeks the transplant had adhered firmly to the surrounding and underlying tissue and structure.

After five to six weeks, the transplant had loosened to some extent to bare fresh epithelial skin underneath. The patient was discharged on December 20, 1952, in excellent condition. On my last examination August 21, 1956, the patient had good muscle control and exhibited ability to flex and extend both legs and elbow. (Figs. 4 and 5)

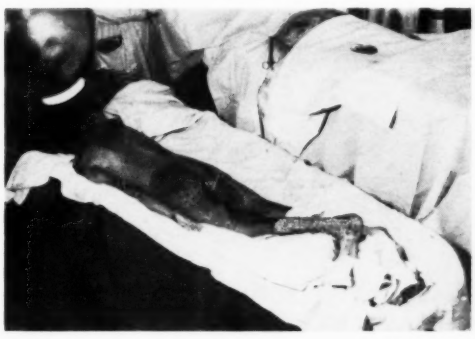

FIGURE 2
Patient during homotransplantation; donor (mother) in background.

FIGURE 3
Close-ups of transplants to left leg.

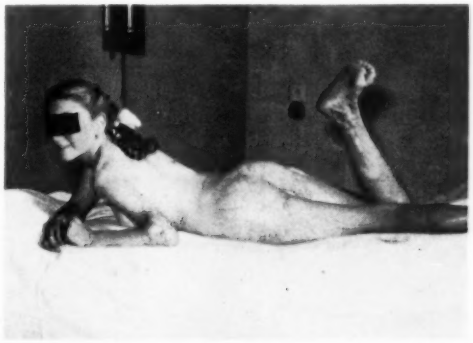

FIGURE 4
Same patient, four years later.

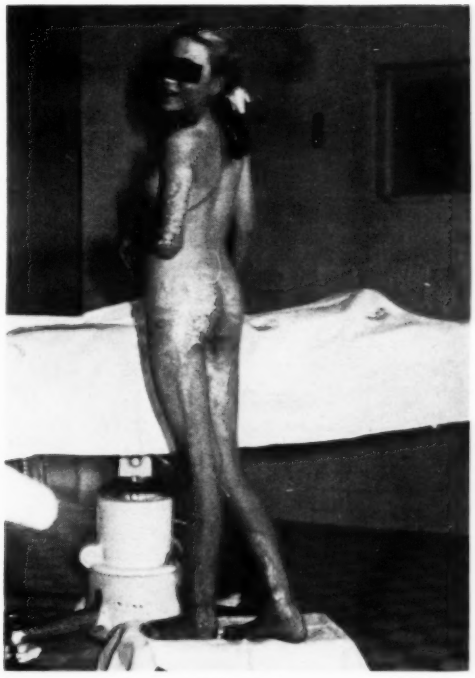

FIGURE 5
Same time as Fig. 4; these demonstrate ability of patient to flex and extend extremities.

SUMMARY AND CONCLUSIONS

The significance of the homotransplantation of the skin is emphasized, and the author also discusses the problem of skin-graft conservation with special reference to the use of sterile amnion originating from normal birth or Caesarean section. Cases from the literature are discussed, as well as one of the author's own cases in which the skin of the mother's abdomen was overplanted with Reverdin plastic on the extensively burned body of the daughter. The author believes that the surgical treatment of deep burns can be effected systematically and expertly through refrigeration and storage of transplantation. Covering is also possible by homotransplantation employing sterile, conserved amnion with temporary success. Although the full value of the amnion membrane is yet to be realized, its immediate use in treatment for extensive burns has been established.

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ATYPICAL ACUTE GLOMERULAR NEPHRITIS IN THE ADULT*

William T. Hall, M. D., Robert W. Frelick, M.D., and Joseph W. Abbiss, M.D.

There appears to be atypical acute glomerular nephritis that may be present with minimal urinary findings, without fever, significant oliguria, hypertension, or edema of the face. While a patient may have acute nephritis without having all of these signs, it is most unusual for all of them to be absent.

CASE REPORT*

A 37 year old, white, married woman was admitted to the Memorial Hospital May 30, 1956, for the third and final admission.

Her first admission was in 1953, at which time a D. and C. was done for uterine bleeding. Admission count was 2.74 million red cells and 5.5 gms. of hemoglobin; W.B.C. 5,700. She received two pints of blood postoperatively and had a febrile reaction after the second pint. Urinalysis: PH6.5; sp. gravity 1.015; alb. and sugar negative; 0-4 WBCs/hpf. Pathological report: Endometrium, follicular phase.

Following this admission she did well for almost a year, but thereafter began to flood again, and by July of 1955 was using three boxes of super-Kotex per period. In 1955, she was admitted for a second D. and C. The admission blood count: R.B.C. 4.09 million; Hgb. 8.3 gms.; Urinalysis: normal. Although on the first admission mention was made of uterine fibroids, no fibroids were found on this admission. The pathological report: Endometrium, late secretary phase. A bone marrow aspiration was done at the operation and was reported as normal. After this admission she was well for three months, but gradually her flow increased. On the period just prior to admission she flooded thirteen days — stopped two days — then flooded five more days. After the first ten days of this period, treatment was begun with Testosterone and Stilbesterol. When they appeared to be ineffective she was admitted to the hospital.

Past Medical History: In 1951 she had a typical duodenal ulcer which was confirmed by x-ray. The symptoms recurred in 1955 and responded satisfactorily to treatment. There was hyper-acidity present with the free hydrochloric acid up to 56°. For at least ten years she had a low-grade hypochromic anemia which was at times normocytic and at others microcytic. Oral iron tended to upset her ulcer, and intravenous iron (40 mgs. Proferrin per week) caused fainting and dizziness. In 1952 she had had an attack of Meniere's Disease which lasted six months. There had been a left mastoid operation at age one.

Physical Examination: The patient was a slightly obese, pale-skinned, white female. B.P. 138/80. Pulse 74. Resp. 20.

Heart, lungs, abdomen, and extremities were negative. Vaginal examination revealed a tiny cervical polyp and an irregularly enlarged corpus.

Admission laboratory data revealed: R.B.C. 2.92 million; Hgb. 8.5gms.; W.B.C. 7,500; Segs. 84%; Non-segs. 5%; Lymphs. 10%; Eosin. 1%; Hematocrit 32%. Urinalysis: Yellow; PH7 reaction; sp. grav. 1.011; neg. sugar and alb.; 20-30 sq. epith. cells; 0-2 WBCs/hpf.; Kline negative.

Hospital Course: (Figure 1) In her first five hospital days she received four blood transfusions with febrile reactions on the first and fourth. After the second transfusion she was noted to have pain in the right loin of which she continued to complain. On the second hospital day she

* From the Memorial Hospital, Wilmington, Del.

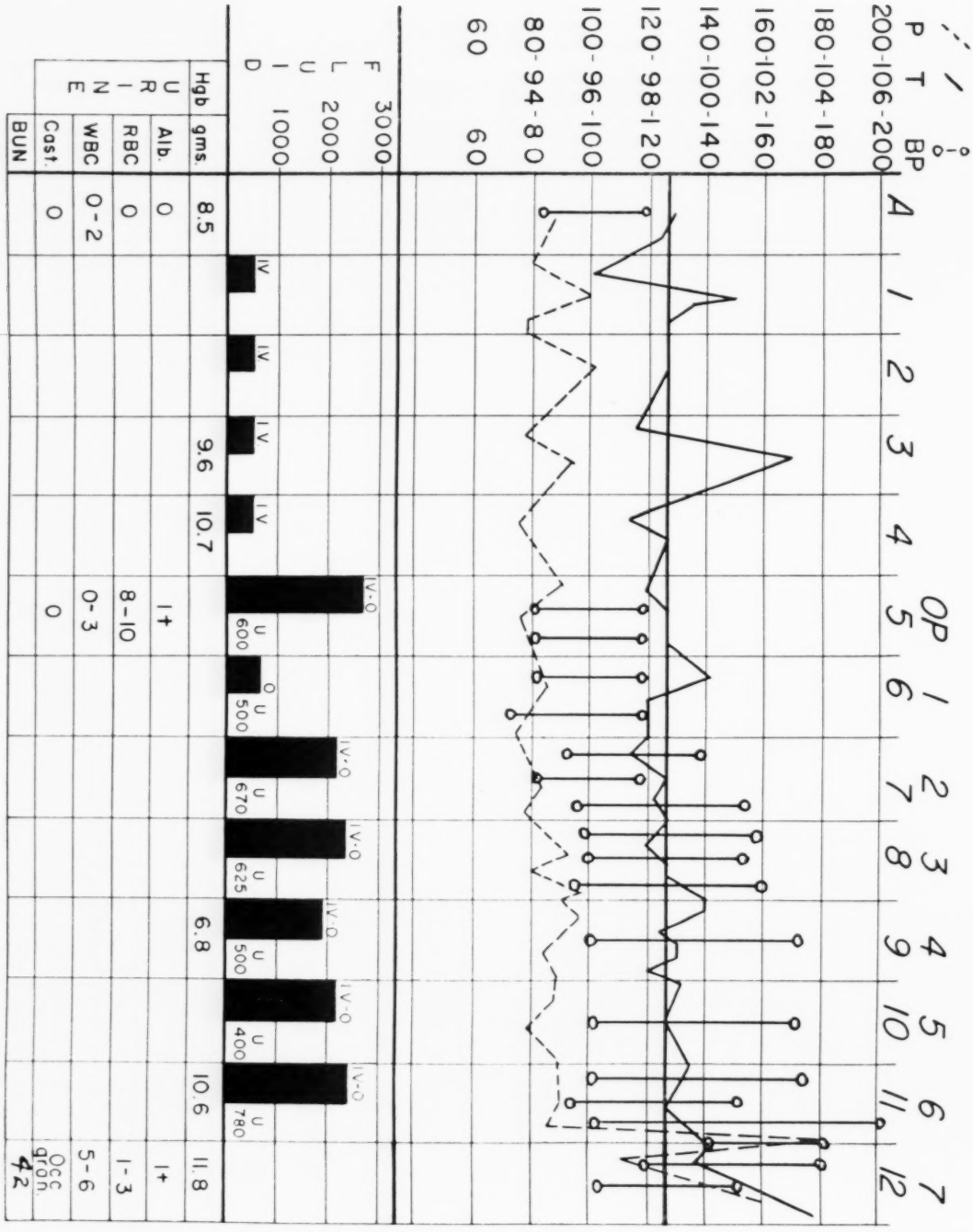
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Figure 1

metaphosphate produced markedly higher blood levels than capsules containing either the corresponding base or the hydrochloride alone. In addition, the average levels derived from the tetracycline base or the chlortetracycline base were higher than those produced by the corresponding hydrochloride though lower than those resulting from the mixture containing the base and sodium metaphosphate. In the study with chlortetracycline[6] capsules containing a mixture of the hydrochloride and sodium metaphosphate were also included in the crossover, and the average levels produced by these capsules were the same as with the mixture of chlortetracycline base with sodium metaphosphate.

Although the enhancement of blood levels of tetracycline by phosphate, either complexed to the tetracycline or mixed with the base or the hydrochloride, thus seemed fairly well established, some doubts still remained because certain reliable observers (including many whose results have not been published) failed to confirm the findings with the materials and methods they used. Further confusion seemed to be added by a subsequent report of Welch et al.,[7] who, in repeating a crossover study with capsules of tetracycline phosphate complex and tetracycline hydrochloride with and without sodium metaphosphate, found much hi[illegible]

"...Tetracycline hydrochloride and citric acid, in an encapsulated mixture, produced higher serum concentrations and greater urinary excretions, and hence better absorption of tetracyclines, than any other preparation studied..."

[illegible] addendum to the last mentioned paper of [illegible] et al.[7] indicates that in their study the capsules of tetracycline hydrochloride, chlortetracycline hydrochloride and tetracycline phosphate complex all contained dicalcium phosphate as a filler, whereas the capsules containing citric acid and sodium hexametaphosphate did not contain any dicalcium phosphate. This could clearly explain the discrepancies noted in that study. Likewise, the inconsistencies in other studies may very well have been due to the presence of calcium as fillers in some of the capsules and not in others.

This, however, fails to explain the most recent findings of Welch and Wright,[10] who compared the absorption of three capsules, each containing 250 mg. of oxytetracycline hydrochloride — one without any adjuvant, one with 250 mg. of citric acid and the third with 380 mg. of sodium hexametaphosphate; no other filler was contained in any of these capsules. In triple

[illegible] of sodium [illegible] were published simultaneously with the last mentioned report of Welch et al.[7] These data were based on thoroughly controlled studies both in rats[8] and in man[9] and include additional findings that serve to explain, fairly conclusively, the various discrepancies that have been mentioned.

The experiments in rats[8] were carried out to study the effects of citric acid, dicalcium phosphate, sodium metaphosphate, food, oil and sorbitol on the serum antibacterial activity produced by the administration of tetracycline hydrochloride or tetracycline base. Citric acid administered in equal weight with tetracycline hydrochloride gave the highest concentrations of all the preparations studied. No enhancing effect was obtained from citric acid when given with tetracycline base. Dicalcium phosphate and food resulted in lower, and sodium metaphosphate in higher, serum antibacterial activity than was observed in their absence. Oil and sorbitol did not interfere with tetracycline absorption.

Dicalcium phosphate is widely used as a filler in various capsules, including those of the tetracyclines. The authors cite a large number of other studies that implicate the presence of calcium ions as the cause of the reduced absorption of tetracyclines and show that citric acid can partially neutralize this effect. The depressing effect of food on the serum levels of tetracycline is likewise explained by the goodly amount of minerals contained in commercial laboratory diets, and they postulate that the multivalent cations may be responsible for the poorer absorption of the drug. The authors could not explain the failure of citric acid to enhance serum concentrations when administered with tetracycline base in contrast to its marked effect when given as the hydrochloride. However, they hypothesized that the ability of citric acid to enhance serum levels of tetracycline is related to its ability to form complexes [illegible] unavailable for [illegible]

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The New England Journal of Medicine.
258:97-99, (January 9) 1958

slipped and fell in the bathroom; there was some question as to whether she became unconscious.

On June 3: R.B.C. 4.48 million; Hgb. 10.7 gms. cathererized specimen on that day revealed: sp. grav. 1.009; PH5; alb. 1+ sugar neg.; 3+ sq. epith. cells; 8-10 RBCs and 0-3 WBCs/hpf.

The diagnosis was made of hemorrhage from a fibroid tumor of the endometrium and surgery was performed on June 3rd. Approximately 500 to 600 cc. of dark, hemorrhagic fluid were found in the pelvis. The right ovary measured about 5 cms. in diameter and contained a large chocolate cyst. The left ovary measured 3 to 4 cms. in diameter and also contained old blood. The uterus was approximately normal in size and contained a submucous fibroid measuring about 3½cms. in diameter. Palpation of the left kidney revealed the presence of a cystic tumor mass in the lower pole which measured about 4 cms. in diameter. The gallbladder was tensely distended, but no calculi were palpable within it. The right kidney was normal to palpation. During surgery the patient received 500 ccs. of blood without reaction.

On the first postoperative day her dressings became soaked with blood and she became weak and nauseated and very nervous; however, her abdomen was soft, and peristaltic sounds were normal. She fainted the first time she was out of bed on her second postoperative day. The third postoperative day she became nauseated, and it was noted that her diastolic pressure had risen to 100, but it fell to 80 later on in the day. Thereafter the blood pressure gradually increased to 160/100. On June 8 the hemoglobin was reported to be 6.8 grams, and she received a pint of blood on that day and another the following day. In spite of adequate fluid intake she continued to have a low urinary output of 500 to 670 cc. On June 10 she became orthopneic but her lungs were clear to auscultation. The pulse rate was 95. At 10:59 P.M. on June 10 she had a convulsion in which she first stared straight ahead, then the eyes looked off to the left, and tonic movements began in the right arm without a clonic phase but with complete loss of consciousness. There were three more convulsions between 10:59 and 1:10 A.M., and this time it was noted she was in pulmonary edema. Positive pressure oxygen was begun, and she received 1.2 mgs. of Cedilanid intravenously, Aminophylin by vein, and intramuscular Dilantin as well as barbiturates and intravenous sodium amytal. The following morning studies were as follows:

Urinalysis: sp. grav. 1.001; PH5; alb. 1+; sugar neg.; moderate epith. cells; 1-3 RBCs and 5-6 WBCs/hpf.; granular casts.

Blood Count: R.B.C. 3.85 million; Hgb. 11.8 gms.; W.B.C. 37,000; Segs. 73%; Non-segs. 19%; Lymphs. 8%; Platelets 554,000.

Blood Urea Nitrogen: 62.2 mgs.%

CO_2 :41.2 volumes %.

Chlorides: 103.7 milleq.

Sodium: 126 milleq./liter.

Potassium: 5.25 milleq.

At 7:35 P.M. her fifth convulsion occurred during which she expired. She had been relatively afebrile except for the two transfusion reactions and a fever that began in her last eight hours of life, 101 to 102 degrees. With the convulsions the pulse increased to 180 on one occasion then dropped down in the post-ictal stage to 110 but rose gradually to 140 and 156 just prior to death.

Post Mortem Examination: Brain: Weight was 1,410 grams and showed moderate edema. Each pleural cavity contained 1000ccs. of clear, straw-colored fluid. The right lung weighed 1000 grams; the left, 750 grams. There was severe hemorrhagic edema without pneumonia, tumor, infarction, or abscess formation. The heart weighed 380 grams. The coronary arteries revealed them to be grossly normal. The heart revealed no valvular disease. There was some dilation of the right auricle and ventricle. The myocardium revealed no evidence of old or recent myocardial infarction. Peritoneal cavity: On opening the peritoneal cavity approximately 150 to 200

ccs. of light, sero-sanginous fluid was found to be present. No evidence of peritonitis was found. The gallbladder was normal. The liver weighed 1,650 grams and showed marked congestion with accentuation of the normal hepatic architecture. The spleen weighed 220 grams, quite firm on sectioning, and was found to be markedly congested. The pancreas was normal, as was the gastro-intestinal tract. The adrenal glands were also normal. There was no enlargement of the kidneys; each kidney weighed 180 grams. Capsule stripped with ease and revealed large, pale kidneys which were rather flabby in consistency. This severe pallor to be sharply limited to the cortex. The pyramids were striated, being alternately gray and red. There was no evidence of tumor formation, of stone, or pyelonephritis, nor of hydronephrosis. There was no increase in peripelvic fat. The ureters were not dilated, and the urinary bladder presented no gross abnormalities.

The uterus, fallopian tubes, and the ovaries were absent, and the peritoneum was closed with sutures over the site of their usual location. External genitalia were normal. The lymph nodes were normal. Bone marrow section and bone marrow presented no gross abnormalities.

Microscopic Examination: Lungs: The lungs show marked congestion together with edema. Many of the alveoli contain large macrophages containing blood pigments, so-called heart failure cells. Sections taken from various sections of the brain show some edema. The spleen is markedly congested. The myocardium, pancreas, and adrenal glands are normal. Kidneys: The histology of the kidneys is striking (See Figure 2). The glomeruli are diffusely affected and show proliferation in Bowman's-Capsule together with proliferative changes in the capillary tufts, many of which almost completely fill the glomerular space. In addition, exudative changes are present within the glomeruli, red blood cells, and protein material lying in the glomerular space. Red blood cells are noted in the proximal renal tubules. There are very

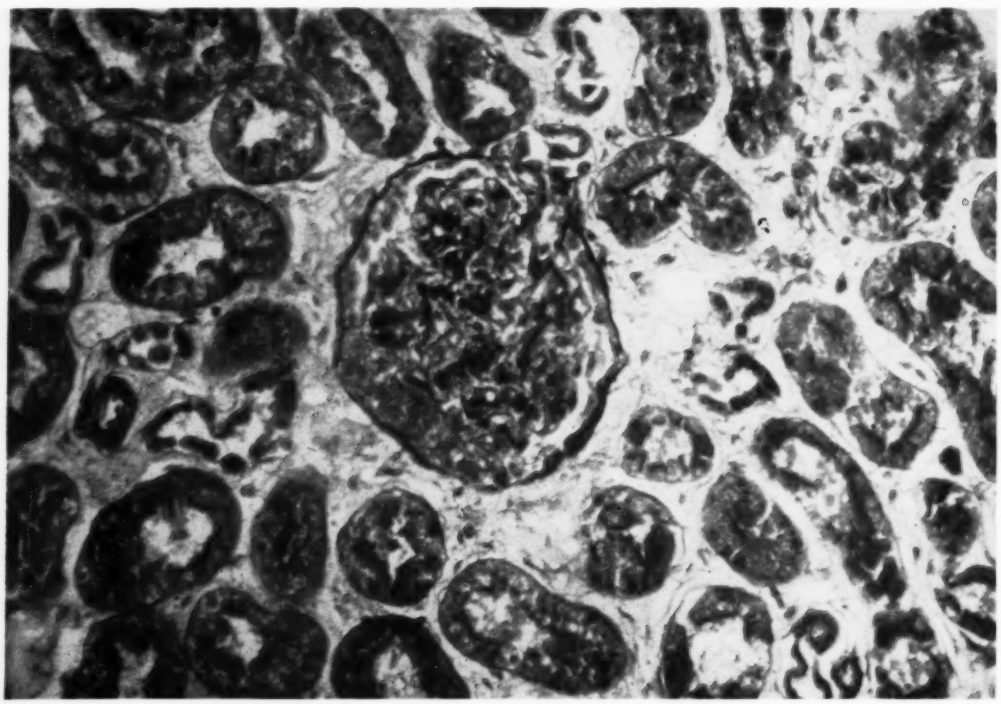

FIGURE 2
Section of kidney showing swollen capillary tuft, thickening of Bowman's capsule and exudate within glomerulus.

marked post-mortem changes in the renal tubules, but in addition some of the tubules show ante-mortem degenerative changes. The features are those of acute diffuse glomerulonephritis.

Patholigical Diagnoses: Acute diffuse glomerulonephritis with uremia.

Total hysterectomy and bilateral salpingo-oophorectomy
(status postoperative eight days)

Myocardial decompensation, pulmonary edema, and congestion with passive congestion of liver and spleen.

Although the diagnosis of glomerulonephritis was mentioned ante-mortem, it was not considered seriously by the ten physicians who saw her during her final hospitalization. The reasons given were the lack of any previous renal symptoms (nocturia, dysuria, frequency, etc.); the normal urine studies over the past two to three years (these were only office and hospital urinalyses); the minimal changes in the urine; the absence of edema (or possibly its masking by her pallor from the anemia and her moderate obesity); and the rather insidious onset of the oliguria in the postoperative period.

A niece had developed an attack of acute nephritis approximately two weeks before the patient entered the hospital. However, members of the two previous generations on the other side of the niece's family had succumbed to glomerulonephritis which appeared to put the heredity trait very definitely out of our patient's family.

We reviewed the charts of patients ten years of age and older with acute glomerulonephritis at the Delaware Hospital and the Memorial Hospital in this City from January, 1950, to June, 1956, and these will be reported in detail at a later date. Our most significant findings demonstrated that out of fourteen deaths, twelve died with diagnoses other than glomerulonephritis, and in eleven there is no evidence from the charts that the diagnoses were considered ante-mortem. Within the past two years Dr. S. S. Bjornson, Medical Examiner of the State of Delaware, has found four more cases of acute glomerulonephritis among patients dying of unknown causes. Two other cases have also appeared in the last six months on the hospital wards. In all these the diagnosis was not suspected ante-mortem.

It may well be that there is a type of acute nephritis which progresses rapidly to death and about which little can be done. However, the low index of suspicion and the high mortality among these cases give us hope that with earlier recognition more rational therapy can be planned. The diagnosis should be suspected in any patient who is not doing well. Appropriate urine studies, BUNs, and a careful intake and output record should be kept. As in renal insufficiency from any other cause, electrolyte fluid and protein balance are the mainstay of treatment. Anti-hypertensives, analeptic drugs, and adequate rest are important. The part the artificial kidney will play in this phase of nephritis is yet to be determined.

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HEARING AIDS: INHERENT DANGERS IN FITTING

J. ROBERT FOX, M.D.*

There has been an increasing trend for the person who is hard of hearing to purchase a hearing aid directly from a salesman, either in his home or over the counter of a drug, jewelry, or department store. The following case reports illustrate the importance of a careful evaluation of the patient who presents himself with the complaint of deafness. In each history the symptom of depressed hearing represented a partial deafness in only one ear. There had been no catastrophic illness, no otorrhea, no otalgia and the patient could have just as easily sought the advise of a hearing aid salesman as an otologist. The difference in outcome, had the former been chosen for consultation, is the point I wish to make.

A 63 year old white man, developed deafness and tinnitis in the right ear one month prior to examination. Self administered irrigation of cerumen from his external canals had failed to give any relief. Both tympanic membranes were of normal color and clearly visible through cerumen free canals. The right tympanum was considerably more retracted than the left. Anterior nares were clear. The oropharynx showed clean tonsil fossae. The neck was negative for lymphadinopathy. Examination of the nasopharynx prior to cathaterization and inflation of the Eustachian tubes showed a small white mass superior to the right Eustachian orifice. This area at first glance through the nasopharyngoscope appeared to be purulent secretion but manipulation with a cotton tipped applicator indicated this was necrotic tissue. Cathaterization and inflation was carried out with transient improvement in the hearing of the right ear, suggesting that compression of the Eustachian tube had accounted for the retracted right tympanic membrane and deafness. Next a biopsy was taken from the white mass and sent for microscopic study. Dr. O. J. Pollak, Pathologist of the Kent General Hospital, reported a malignant epithelioma. A high degree of malignancy was indicated by a large number of mitotic figures and accounted for the superficial necrosis. Following the biopsy report, Dr. E. R. McNinch, Radiologist of the Kent General Hospital, examined this lesion through the nasopharyngoscope and advised roentgen therapy.

The second patient was a 56 year old white man who was told by his family that his hearing was deteriorating in both ears but particularly in his right ear. His childhood history indicated repeated attacks of otorrhea although no acute ear disease had occurred in the past few years. Examination of the ears revealed clear canals and moderately scarred tympanic membranes with slight retraction. The anterior nares were clear. A view of the nasopharynx showed a large fibrous polyp protruding into the right nasopharynx and covering the right Eustachian orifice. An audiogram showed an air conduction loss in the right ear of 30-35 db. in the lower frequencies dropping to 80 db. at 4000. The left ear averaged 15 db. loss. Removal of the polyp restored the hearing in the right ear to a 15 db. loss for lower frequencies although the high tone loss remained unchanged. Microscopic report by Dr. O. J. Pollak, Pathologist, was fibrous polyp, non malignant.

The above facts lead one to conclude that a careful medical examination in the problem of deafness should be a prerequisite to the fitting of a hearing aid. Had either of these patients gone directly to a hearing aid salesman, the organic lesions that represented the primary etiology would have

* Dover, Delaware.

been overlooked. In the instance of the nasopharyngeal malignancy, any delay in recognizing this tumor and instituting the correct therapy would have unmeasurably decreased the patient's chances for survival.

There is no ready answer to the problem of divided responsibility to the deaf patient. A solution could resolve out of a better appreciation on the part of the hearing aid manufacturer and his representatives as to the true scope of their activity. Non professional advice on medical problems can reach a point beyond which it becomes a detriment rather than an aid to the patient. Accepting a full share of responsibility to the deafened would result in fewer failures in fitting hearing aids and surely uncover a number of contributing causes that could be improved with treatment. An effort should be made in advertising and sales techniques to direct the hard of hearing to an Otologist for evaluation before a hearing aid is sold.

SUMMARY

(1) Examination by an Otologist should precede the fitting of a hearing aid.

(2) Two examples of organic lesions causing deafness for which hearing aids were not indicated were cited.

(3) Greater responsibility to the patient on the part of the hearing aid manufacturer and his representatives was recommended.

IN THE SUPREME COURT OF THE STATE OF DELAWARE

BARBARA LYNN CHRISTIAN, an infant, by her next friend, JAMES A. CHRISTIAN,

Plaintiff Below,

Appellant,

-vs-

WILMINGTON GENERAL HOSPITAL ASSOCIATION, INC., a corporation of the State of Delaware,

Defendant Below,

Appellee.

No. 23, 1957

(November 8, 1957)

SOUTHERLAND, C.J., WOLCOTT and BRAMHALL, JJ., sitting.

Writ of Error to the Superior Court of New Castle County.

Donald W. Booker, of Wilmington, for appellant.

E. N. Carpenter, II, of Wilmington, for appellee.

WOLCOTT, J.:

This appeal seeks reversal of a directed verdict for the defendant at the close of the plaintiff's testimony in the trial of an action before the Superior Court against the defendant hospital, based on the alleged negligence of its agent.

The facts may be stated as follows: The plaintiff, in January, 1953, the time of the injury, was approximately sixteen months of age and, while playing in her home, fell on a glass bottle which broke and cut her hand severely. The plaintiff was taken by her parents to the Wilmington General Hospital and there treated by an intern then on duty in the emergency ward. At the time of treatment, the plaintiff was crying and struggling so that she had to be held by her parents and a student nurse then on duty.

The intern examined the wound, treated it and sewed it up and, in response to a question by the infant's father, stated that the tendons of the hand were not severed. Later, although the testimony is somewhat confused as to the exact time, the plaintiff was again taken to the defendant hospital. This subsequent visit was either four or ten days following the accident. She was again examined by the same intern who noted that a stiffness had developed in the index finger of her right hand. At this time the intern did not diagnose the stiffness as having been caused by a severed tendon, although, again on this point, the testimony is confused.

Subsequently, a third time, the plaintiff was taken to the defendant hospital and, at this time, the plaintiff's parents may have been advised that the stiffness in the index finger was caused by a severed tendon. In any event, however, in April, 1953, the plaintiff was examined at the Philadelphia Naval Hospital and her parents advised that the tendon serving the index finger of her right hand had been severed, and that an operation would be required to repair it. As of the date of trial of this cause, approximately four years following the injury, the operation has not been performed.

The plaintiff called as witnesses two doctors to testify as experts. The substance

of their testimony with respect to injuries of this type and the treatment customarily followed is set out. In a child of this age the tendon leading to an index finger is approximately the size of a heavy piece of string, perhaps as much as ⅛ inch in diameter. By visual examination of the wound, it is possible to see the tendon if it has not been severed, but it is also entirely possible, in the case of a small struggling and crying child, that the tendon would not be seen. In the treatment of such a wound, it is routine practice to determine if possible whether or not tendons have been severed, but if the child is uncooperative, it is oftentimes impossible to determine because diagnosis requires flexion of the finger which, in turn, can be achieved only by the cooperation of the patient.

The doctors testified that when a tendon is divided an operation is invariably required to repair it since a severed tendon will not grow together of its own volition, but tends to withdraw into the wrist after having been severed. They also testified that an immediate operation for a severed tendon is not always performed. Whether or not immediate repair is made, or the operation postponed depends upon a number of factors, such as possible contamination of the wound and, also, in the case of a small child the desirability of permitting normal growth to take place to make subsequent repair by operation easier.

The doctors were agreed that immediate operation is not necessary for the repair of a severed tendon and that postponement of the operation, even for as long as four years, would not result in any permanent disability by reason of the delay. In other words, successful repair of a severed tendon can be made after the lapse of years.

The doctors also testified it was possible, at the time of the initial examination by the intern, that the tendon leading to plaintiff's right index finger was only partially severed, which would not have been discovered by examination, and that the tendon might have ruptured later after the initial treatment, which, if that were the fact, would not have been the cause of the rupture.

Upon this state of the plaintiff's evidence the trial court instructed the jury to return a verdict for the defendant on the ground that is was insufficient to establish a *prima facie* case in the plaintiff's favor because of two deficiencies. The first deficiency was that there was no evidence at all that the intern employed by the defendant had failed to conform to accepted standards of care and treatment prescribed for physicians in the community. And the second deficiency was that there was no evidence offered by the plaintiff that the treatment performed by the intern was the proximate cause of the injury.

Plaintiff now appeals, making two basic arguments for the reversal of the directed verdict, viz., (1) that the plaintiff did offer sufficient evidence of the failure of the intern to conform to the accepted medical standards in the community for the care and treatment of injuries of the nature suffered by the plaintiff; and (2) that in any event the case should have been submitted to the jury by reason of the doctrine of *res ipsa loquitur*.

As a general proposition, a physician, surgeon or dentist is answerable in damages for an injury to a patient resulting from his failure to use the standard knowledge and skill required of doctors, or by reason of his failure to use reasonable care and diligence in the application of such knowledge or skill. 41 *Am.Jur., Surgeons and Physicians*, §104; 70 *C.J.S., Physicians and Surgeons*, §48. However, as in every action based upon negligence, negligence is not presumed but must be affirmatively proven. This proposition is so elementary as to require no citation of authority. Nor does the sole fact that an injury has resulted from a certain treatment raise any presumption of negligence on the part of the attending doctor. See cases annotation, 162 *A.L.R.* 1278.

It is therefore incumbent upon a plaintiff seeking recovery for injury upon the theory that that injury has resulted from faulty medical care given by a doctor to prove the medical standards to which that doctor is required to conform. In almost all cases this standard necessarily must be

established by competent expert testimony since only in the most superficial way can laymen be expected to know the appropriate standards of care to be followed.

In this case the plaintiff attempted to establish the standard which should have been complied with. This was done by the testimony of two admitted experts in the field of treatment of injuries of this nature. It is clear from their testimony that is was entirely possible in examining this patient according to that standard not to ascertain at the time of such examination that a tendon had been severed. It is furthermore clear that the failure to ascertain immediately the severing of the tendon did not result from a failure to conform to the accepted standard and, in any event, that no permanent injury has followed the failure to discover the condition.

It seems clear from the plaintiff's case that the intern at the defendant hospital examined the infant plaintiff as any other doctor in the community would have examined her under like circumstances. There is no evidence that his treatment of the wound and suturing failed in any respect to conform to the established standards for the medical profession.

This being the state of the evidence it is the law that a presumption arises that the doctor in fact exercised ordinary and reasonable care and prudence in the treatment of the wound, when there is no direct evidence to the contrary. *Mitchell v. Atkins*, 6 W.W.Harr. 451, 178 A. 593; 41 *Am.Jur., Physicians and Surgeons*, §127.

We are of the opinion, therefore, that the plaintiff failed to produce affirmative evidence of negligence by direct testimony sufficient to require the trial court to submit the issue of negligence to the jury for its determination.

In this connection appellant argues that it is not necessary to prove the standard of care required of doctors by the testimony of other doctors because of what is said to be an unwillingness on the part of one doctor to charge his professional brother with negligence. It is, of course, obvious that in some instances a jury of laymen could determine without the testimony of experts that a treatment given was so unrelated to the injury or illness of the patient as to make obvious to anyone the failure of the doctor to exercise acceptable standards of care. But, in the ordinary case of bodily injury, the proper treatment of which would not be known to a layman, we think it necessary to offer the testimony of admitted experts for the guidance of the jury in determining the issue of negligence or non-negligence. In our opinion, the injury of which this plaintiff complains was of such nature as to require a method of treatment not obvious enough to warrant the assumption that a layman, in the absence of expert testimony on the subject, could make an intelligent decision upon the propriety of the treatment given.

Secondly, the plaintiff argues that the issue of negligence should have been submitted to the jury because of the doctrine of *res ipsa loquitur*. This court's predecessor, in *Delaware Coach Co. v. Reynolds*, 6 Terry 226, 71 A.2d 69, stated that the doctrine of *res ipsa loquitur* is available to a plaintiff to take his case to the jury "where the facts and circumstances surrounding the occurrence of the injury warrant the interference of negligence on the part of the defendant". The court went on to say that in order to determine the availability of the doctrine the court must examine the manner in which the alleged injury occurred and then determine whether or not in the usual course of events it would be concluded by reasonable persons that the injury would probably not have occurred except for some negligence on the part of the defendant.

In *Mitchell v. Atkins*, supra, a case seeking to make a dentist respond in damages for the death of a patient in the circumstance that, while extracting a tooth, gas was administered as an anesthetic under the influence of which the patient died, it was held that a count in the declaration alleging no negligence but relying solely upon the doctrine of *res ipsa loquitur* based upon the fact of administration of an anesthetic and subsequent death, was subject to demurrer for failing to state a cause

of action. The court went on to say that it was necessary in such actions to prove a lack of requisite knowledge or skill, or a failure to exercise such, or the use of some instrumentality in treatment of the patient which results in something so inconsistent with the normal and usual result that negligence in the application of the instrument must be pre-supposed.

This case in its best light for the plaintiff is, at most, one of an unfavorable result from the treatment employed. It seems clear in such circumstance that, based upon the unfavorable nature of the result of treatment, no presumption of negligence on the part of the doctor can arise. See *Annotation*, 162 *A.L.R.* 1281; *Mitchell v. Atkins*, supra; 38 *Am.Jur., Negligence*, §295.

We are of the opinion, therefore, that the trial court was correct in refusing to submit the issue to the jury on the doctrine of *res ipsa loquitur.*

The foregoing is sufficient to affirm the judgment below. We are not called upon, therefore, to pass upon the additional question of whether or not the plaintiff had successfully shown any casual connection between the treatment given by the intern and the injury. We content ourselves in this respect with saying that we think it clear that the treatment given did not and could not have caused the stiffness in the plaintiff's index finger. That stiffness was caused solely by the severing of the tendon, which was caused in turn by the cut inflicted by the broken bottle and not be the treatment given the plaintiff at the hospital.

The judgment below is affirmed.

WOMAN'S AUXILIARY

REPORT OF THE MENTAL HEALTH COMMITTEE OF THE WOMAN'S AUXILIARY TO THE MEDICAL SOCIETY OF DELAWARE

The Mental Health Committee of the Woman's Auxiliary to the Medical Society of Delaware has had a very rewarding year.

In New Castle County, a program was devoted to Mental Health this fall. As a result, there are eighteen volunteers from the Woman's Auxiliary working in the State Hospital at Farnhurst three days a week, taking the library carts into the wards.

Two hundred and twenty-five dollars has been designated from the New Castle County group for library supplies. Two hundred and thirty-eight books and numerous magazines have also been donated by this group.

Volunteers have been working in the library cleaning out shelves and unserviceable books. These books will be salvaged for the price the paper will bring.

Recently there have been some pictures taken of volunteers working in the library. These will be used for newspaper publicity.

The State Hospital at Farnhurst is indeed grateful for the efforts of the Woman's Auxiliary to the New Castle County Medical Society.

In Sussex County, the group has been very active in providing toys and books for the hospital for the mentally retarded at Stockley. This is fulfilling a great need. A check for twenty-five dollars has been drawn from the Sussex Treasury and earmarked for the Stockley patients for Easter.

This group has also been sending several local newspapers to the State Hospital at Farnhurst to be used on the library carts. This is of great benefit to the patients in the State Hospital from the lower Delaware counties.

There has been no activity in the Mental Health field in Kent County this year. The group so far is very small, and finds that it must limit its activities to one field and they chose another project this year.

May I take this opportunity to commend the county chairmen for the excellent job they have done in Mental Health so far this year.

Great strides have been made in this too long neglected field.

Respectfully submitted,
(Mrs. G. H. H.) Ione T. Garrison,
State Mental Health Chairman.

RAYMOND T. LaRUE, M.D.

Doctor LaRue was born in Gallipolis, Ohio on March 22, 1895 and died while attending a patient in Wilmington on March 17, 1958.

A graduate of the University of Maryland School of Medicine, Dr. LaRue interned at the Delaware Hospital. He practiced for several years in Michigan before returning to Wilmington in the mid-1920's to become Chief of the Genito-Urinary Service at the Delaware Hospital. At the time of his death he was Consultant in Urology at the Delaware Hospital as well as a member of the staffs of St. Francis, Wilmington General, and Delaware State Hospitals.

He was a member of the Medical Society of Delaware and is survived by his wife, Mrs. Rose LaRue.

1957 ANNUAL REPORT — THE COMMITTEE FOR THE IMPROVEMENT OF PATIENT CARE

HISTORY

The Committee has been meeting regularly for the past three years since its inception on a local basis. It was originally patterned after a national group and is concerned with bringing together physicians, nurses and hospital administrators to discuss problems of mutual interest toward the improvement of patient care.

OBJECTIVES

1. To evolve logical conclusions and to make definite recommendations to parent groups concerning subjects selected for discussion, study and investigation.
2. To review problems of mutual concern and interest to the nurse, the hospital administrator and the physician that arise from the care of the patient.
3. To develop better insight into the problems of the allied professions who have a single goal in mind—"The Patient".

The Committee acts as an advisory body and does not have the power to legislate. Findings or recommendations may be accepted or rejected by any of the participating organizations.

During the past year interest in the work of the Committee has lagged somewhat due to the resignation of one of the hospitals, two of the physicians and the practical nurse representative without replacements being named. Attendance has been relatively poor. The appointment of four new physicians has been announced at the end of the year and a pick-up in attendance is expected. New officers were elected and installed at the regular meeting in December.

BUSINESS OF THE COMMITTEE

The outstanding accomplishment of the year was the institute on "Human Relations in the Hospital" which was held on October 21, 1957, in the Hotel du Pont in Wilmington. Two outstanding speakers, Brig. General Don C. Faith and Dr. B. H. Jarman, both of George Washington University, discussed "Basic Elements of Human Relations", "Communications in Human Relations", "Application of Human Relations", and "Motivation of Human Relations" before a group of 128 representatives of hospitals, medical societies, nurses organizations and other allied fields. This institute was planned and activated by the Committee for the Improvement of Patient Care with the approval and sponsorship of the Tri-State Hospital Association.

A Supervisory Training Program was set up by the University of Delaware in conjunction with this Committee and twelve representatives from Delaware Hospital and four from the Memorial Hospital attended the six sessions. There was some difference of opinion as to the value of this program, but it was generally agreed that those in attendance had gained from the experience and had carried over to their work a new philosophy toward their job and fellow workers. The program is expected to be repeated and extended.

The Social Service Exchange and its function with the hospitals was discussed with the hope that more use could be made of this organization in preventing duplication of service in the hospitals and in giving better service, particularly to OPD patients. The extension of activities on the part of this agency is dependent upon community funds and nothing further has developed.

A study of the Private Duty Nurse Registry has been made in an effort to improve the services rendered and to overcome certain weaknesses in the present organization of the Registry. A consultant from the American Nurses Association visited Wilmington and conducted a survey of the local situation and has submitted recommendations. Other changes have also

been suggested by the Directory Committee of the Delaware State Nurses Association. Reorganization plans continue.

Identification of practical nurses on the floors by means of an arm patch was recommended so that all hospitals would have uniform requirements. This is now in effect.

A training program in "Discussion Leading" is under consideration and preliminary details are being worked out with representatives of the Du Pont Company. This program will be offered to the local hospitals.

It was agreed to invite the administrator of the Veterans Hospital to become a member of this committee.

Uniformity in hospital procedures is to be part of future agenda of the meetings and this Committee will endeavor to work in a liaison capacity to coordinate and standardize recommendations of existing working committees from other groups.

Members of the Committee

Hospitals (Association of Delaware Hospitals): Memorial, Mr. Charles E. Vadakin, Chairman; Delaware, Mr. R. R. Griffith; Wilmington General, Mr. Leo G. Schmelzer; St. Francis, Resigned; Secretary, Mr. J. A. Rockwell.

Nursing (Delaware State Nursing Organizations): Delaware State Nursing Association, Miss Dorothy Hufcut, Miss Therese M. Curran, Miss Dorothy B. Ranck; Delaware League for Nursing, Miss Ruth Curry, Vice-Chairman; Delaware Licensed Practical Nurses Association (vacant).

Physicians (New Castle County Medical Society): Memorial, Dr. Edward S. Parvis; Delaware, Dr. Ward W. Briggs; Wilmington General, Dr. David Platt; St. Francis, Dr. Thomas V. Hynes.

Respectfully submitted,

J. A. Rockwell
Secretary

ANNOUNCING A NEW AWARD FOR MEDICAL WRITING

The Editors of MODERN MEDICAL MONOGRAPHS, a quarterly publication, announce an award for the best unpublished manuscript for a short book on a clinical subject in the field of internal medicine. The purpose of this award, which will be known as the MODERN MEDICAL MONOGRAPH AWARD, is to stimulate young physicians to communicate their work in the classical form of the monograph and to achieve high standards of medical writing. The winner of this competition will receive five hundred dollars. In addition, the winning monograph, if found suitable, will be published as a book in the series MODERN MEDICAL MONOGRAPHS. The generosity and cooperation of Dr. Henry M. Stratton, President of Grune and Stratton, Inc., publishers of the series, have made this award possible.

The entries will be judged for style and clarity of expression by a committee of the American Medical Writers' Association and for clinical interest and scientific value by the Editors and Advisory Board of MODERN MEDICAL MONOGRAPHS.

RULES:

1. The author, or authors, must be a graduate physician, less than 40 years of age. Single authorship is preferred, but two co-authors will be acceptable. The name of the medical school from which the author graduated and his date of graduation should be stated.

2. Manuscripts should be submitted in duplicate (original and one copy) by registered mail, postmarked *not later than October 1, 1958*, to Richard H. Orr, M.D., 37 East 67th St., New York 21, New York.

3. The manuscript, including the bibliography, must consist of between 115 and 200 double-spaced typewritten pages with ample margins and not more than 40 illustrations (figures or photographs). For each illustration used, the allowable upper limit of typewritten manuscript pages should be reduced by one.

4. Fishbein's book, "Medical Writing" (third edition), should be followed in preparation of the manuscript, use of abbreviations, and bibliographic form.

Richard H. Orr, M.D.
Consulting Editor

Irving S. Wright, M.D.
Editor-in-Chief

+ Editorials +

FORAND BILL

Last month's issue of the Journal discussed the latest significant proposal to amend the Federal Social Security System to advance the cause of compulsory national health insurance. The Forand Bill (H.R. 9467), which proposes that surgical and hospital service to recipients of Social Security old age and survivors benefits shall henceforth be at government expense, was analysed and related to the continuing movement of which the Wagner-Murray-Dingell Bills were the most significant and frank manifestations.

The American Medical Association has recently mailed to its component State Societies a very interesting reprint of a news story in the New York Times. Headlined "AMA Opposition to U.S. Aid Scored", the article is a summary of a vitriolic attack upon the AMA stand against the Forand Bill, which is unquestionably a virulent threat to private practice. Characterizing it as "witch doctors exorcising the evil spirit, socialized medicine", Eveline M. Burns, Ph.D., told a group representing the American Public Welfare Association that the AMA is taking "a narrow and self-interested view of the social responsibilities of the profession".

Speaking as the President of the National Conference on Social Welfare, Dr. Burns lamented that little progress has been made in the last 10 or 15 years in Social Security, and that the country has moved so slowly toward more complete elimination of so-called "risk areas" which are now the responsibility of the individual. While stating that she believes that nothing short of National Health Service (presumably resembling Britain's) could meet the problem of patient care in the United States, she conceded that this probably would not come soon. Unfortunately, she said, the attitudes of crucial professions have often hampered social legislation.

We find two highly interesting if not encouraging facets of Dr. Burns' address. First of all, Dr. Burns is Professor of Social Work at the New York School of Social Work of Columbia University, and is presumably instilling her more or less bright and dedicated young pupils with her conclusions on the necessity for national compulsory health insurance. We can, therefore, expect increased pressure for this as time goes by. Certainly, this does not imply that Dr. Burns is an isolated phenomenon. It is our impression that compulsory health insurance is a pet subject of social academicians everywhere.

Secondly, and not less important, Dr. Burns has pointed out at least as well as could the Forand Bill's most fervent opponent the dangers inherent in this legislation. The Forand Bill is aimed at chipping away the barrier the medical profession has erected between itself and the precipice of socialism. These politically palatable capsules can kill free medicine as surely as could a single massive dose. It would be the height of fatuity to fail to take a positive, energetic stand against them as they arise.

Several hospitals in Delaware, as well as the American Hospital Association, have officially opposed the Forand Bill. They have recognized that although care for the aged is a major health problem, the Forand approach is neither economically, psychologically nor sociologically justifiable. The Journal views this stand on the part of the hospitals, who certainly are intimately acquainted with the financial problems of the aged ill, with sincere respect.

It is our hope that the medical profes-

sion of Delaware will not be less actively intelligent in informing our Representative-at-Large, Mr. Harry S. Haskell, of our feelings, individual as well as, collective, regarding this pernicious legislation. Mr. Haskell's address is:

Representative Harry S. Haskell
Congress of the United States
House of Representatives
Washington 25, D. C.

KNOW WHEREOF YOU SPEAK—

Insurance is a large and growing business. Rules, regulations, and types of policies sold constantly change.

Recently, physicians in a small Southern town, sincerely and in good faith, advised two of their patients to drop accident and health policies they had been carrying. One patient was diabetic and the other had a myocardial infarction. The physicians reasoned that their patient's histories of disability would prevent them from collecting claims. This advice, although logical and well-intentioned, was erroneous and was a disservice to the patients.

We should be careful to have all facts available before giving advice.

LEGAL DEFINITION

The Supreme Court of the State of Delaware has clearly defined the relative responsibility of the practicing physician, the interne, and the hospital in a decision reprinted in this issue. This decision is of importance to all of us.

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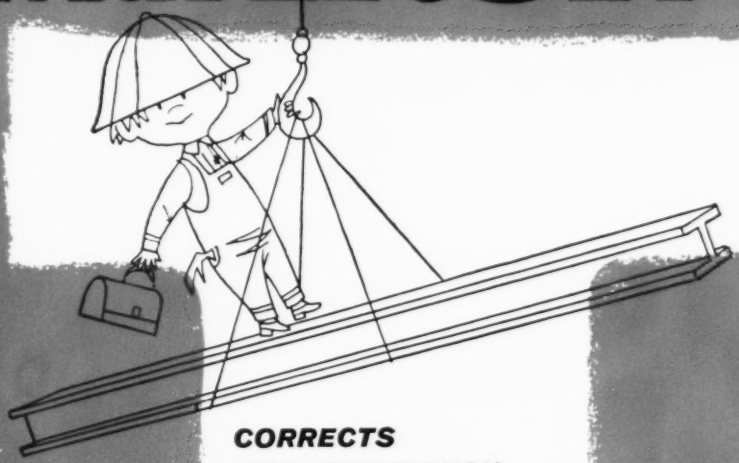

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FORMULA: Each teaspoonful (5 cc.) contains:

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Iron (as Ferric Pyrophosphate)	30 mg.
Vitamin B_{12} Crystalline	25 mcgm.
Thiamine Mononitrate (B_1)	10 mg.
Pyridoxine HCl (B_6)	5 mg.
Alcohol	0.75%

Average dosage is 1 teaspoonful daily.
Available in bottles of 4 fl. oz.

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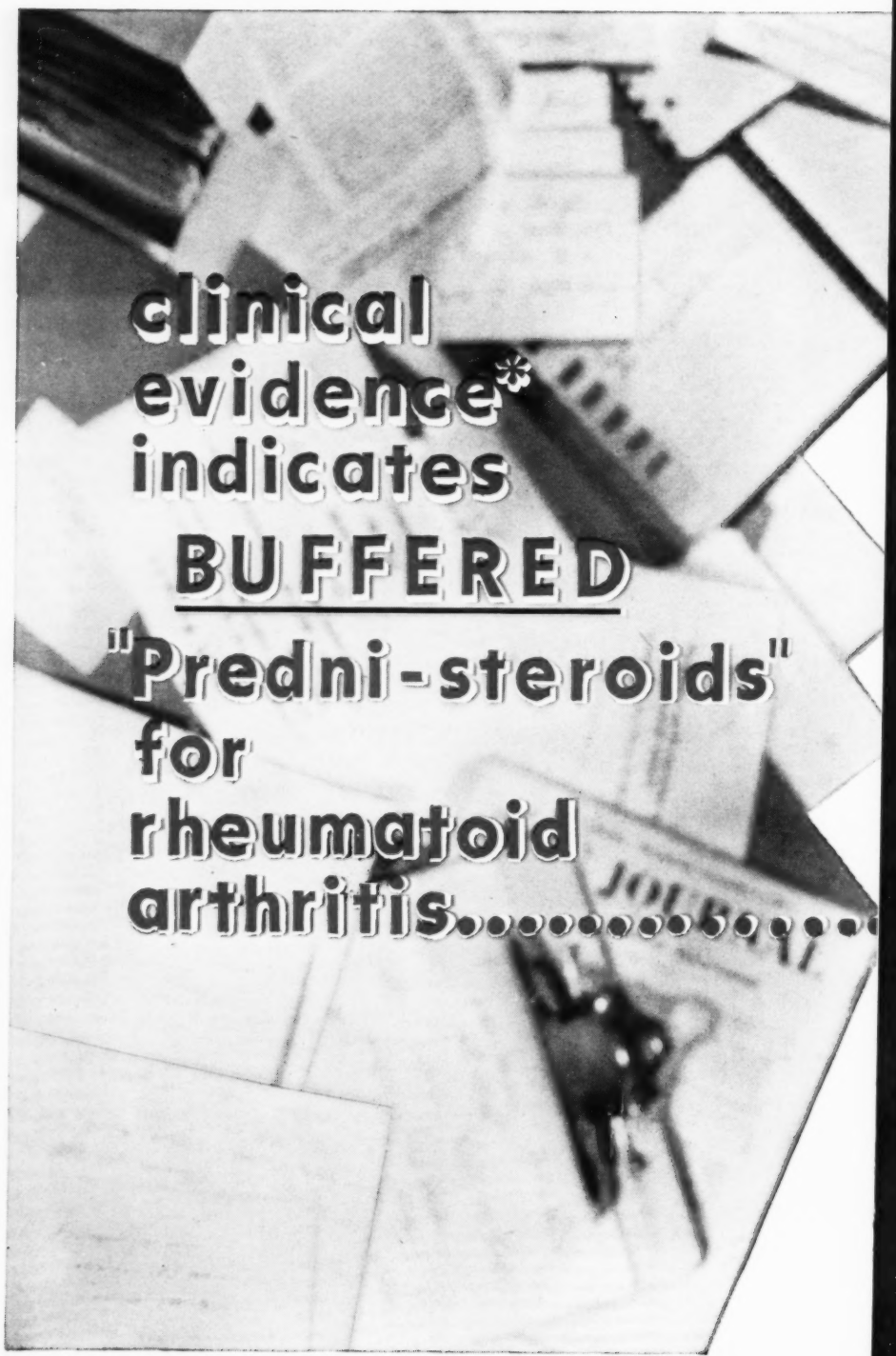
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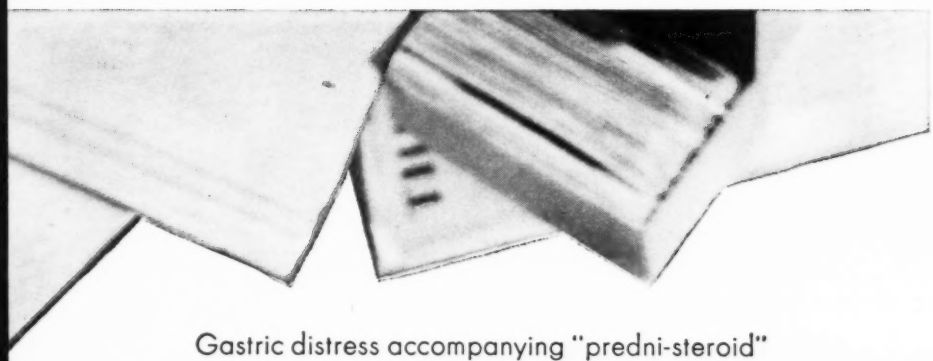

Gastric distress accompanying "predni-steroid" therapy is a definite clinical problem—well documented in a growing body of literature.

*"In view of the beneficial responses observed when antacids and bland diets were used concomitantly with prednisone and prednisolone, we feel that these measures should be employed prophylactically to offset any gastrointestinal side effects."—Dordick, J. R. *et al.*: N. Y. State J. Med. 57:2049 (June 15) 1957.

*"It is our growing conviction that all patients receiving oral steroids should take each dose after food or with adequate buffering with aluminum or magnesium hydroxide preparations."—Sigler, J. W. and Ensign, D. C.: J. Kentucky State M. A. 54:771 (Sept.) 1956.

*"The apparent high incidence of this serious [gastric] side effect in patients receiving prednisone or prednisolone suggests the advisability of routine co-administration of an aluminum hydroxide gel."—Bollet, A. J. and Bunim, J. J.: J. A. M. A. 158:459 (June 11) 1955.

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multiple compressed tablets

provide all the benefits of "Predni-steroid" therapy— plus positive antacid protection against gastric distress

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2.5 mg. or 5.0 mg. of prednisone or prednisolone, plus 300 mg. of dried aluminum hydroxide gel and 50 mg. magnesium trisilicate, in bottles of 30, 100, 500.

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there's pain and inflammation here... it could be mild or severe, acute or chronic, primary or secondary fibrositis—or even early rheumatoid arthritis

more potent and comprehensive treatment than salicylate alone

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more manageable corticosteroid dosage

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Acetylsalicylic acid	325 mg.
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Ascorbic acid	20 mg.

Packaging: SIGMAGEN Tablets, bottles of 100 and 1000.

References: 1. Spies, T. D., et al.: J.A.M.A. 159:645, 1955. 2. Spies, T. D., et al.: Postgrad. Med. 17:1, 1955. 3. Gelli, G., and Della Santa, L.: Minerva Pediat. 7:1456, 1955. 4. Guerra, F.: Fed. Proc. 12:326, 1953. 5. Busse, E. A.: Clin. Med. 2:1105, 1955. 6. Sticker, R. B.: Panel Discussion, Ohio State M. J. 52:1037, 1956.

Acute conditions: Two or three tablets four times daily. After desired response is obtained, gradually reduce daily dosage and then discontinue.

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...from moderate to severe pain complicated by tension, anxiety and restlessness.

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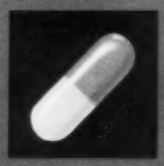

Codeine Phosphate	gr. ¼
Phenobarbital	gr. ¼
Acetophenetidin	gr. 2½
Aspirin (Acetylsalicylic Acid)	gr. 3½

...from pain of muscle and joint origin, simple headache, neuralgia, and the symptoms of the common cold.

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Acetophenetidin	gr. 2½
Aspirin (Acetylsalicylic Acid)	gr. 3½
Caffeine	gr. ½

...from mild pain complicated by tension and restlessness.

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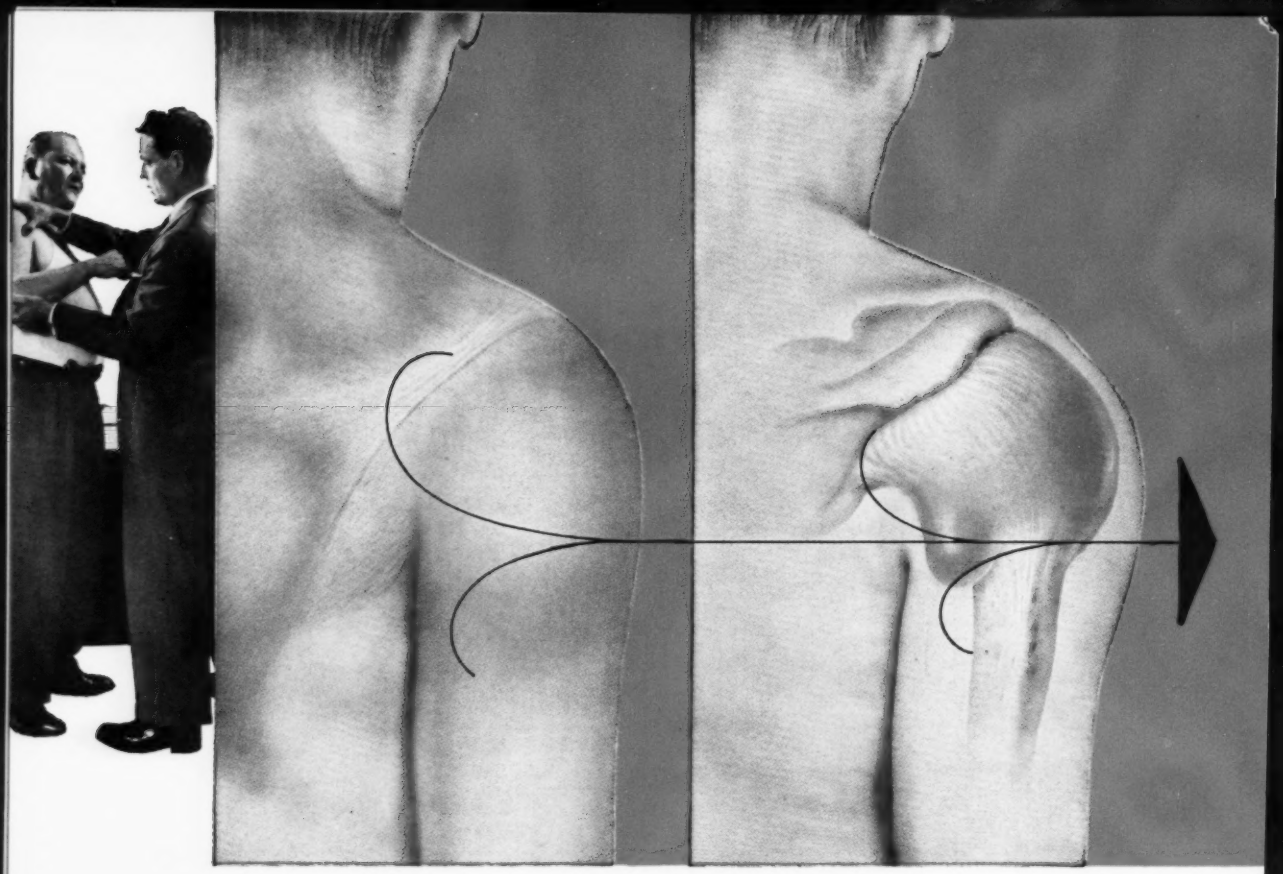
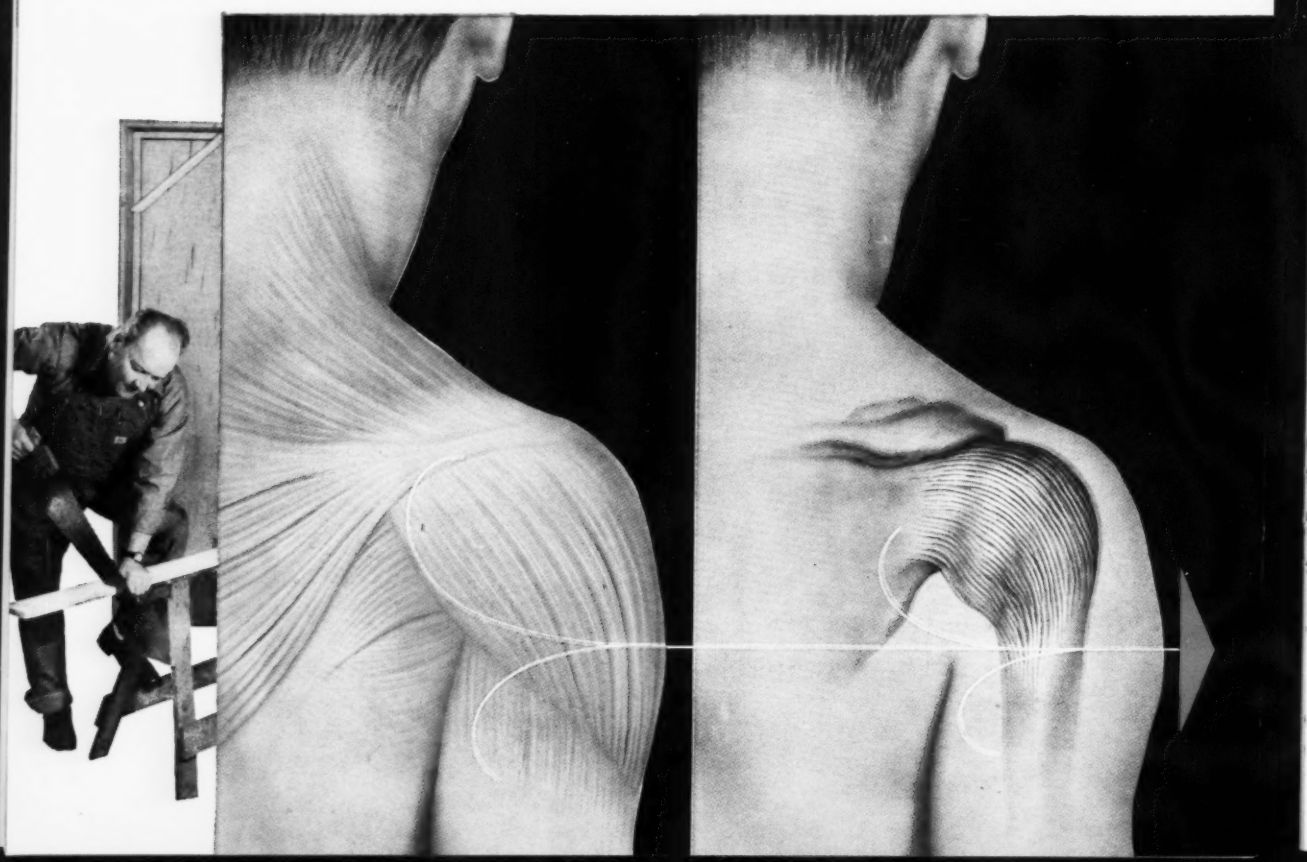
Phenobarbital	gr. ¼
Acetophenetidin	gr. 2½
Aspirin (Acetylsalicylic Acid)	gr. 3½

*Subject to Federal Narcotic Regulations

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York



"Rheumatoid arthritis is a constitutional disease with symptoms affecting chiefly joints and muscles."[1] "Pain in the affected joint is accompanied by splinting of the adjacent muscles, with resultant 'muscle spasm.' "[2]



rheumatoid arthritis involves both joints and muscles

only

MEPROLONE®

THE FIRST MEPROBAMATE PREDNISOLONE THERAPY

meprobamate to relieve muscle spasm
prednisolone to suppress inflammation

MEPROLONE is the only anti-rheumatic-antiarthritic designed to relieve simultaneously (a) muscle spasm (b) joint-muscle inflammation (c) physical distress . . . and may thereby help prevent deformity and disability in more arthritic patients to a greater degree than ever before.

SUPPLIED: Multiple Compressed Tablets in two formulas:
MEPROLONE-2—2.0 mg. prednisolone, 200 mg. meprobamate and 200 mg. dried aluminum hydroxide gel (bottles of 100).
MEPROLONE-1—supplies 1.0 mg. prednisolone in the same formula as MEPROLONE-2 (bottles of 100).

1. Comroe's Arthritis: Hollander, J. L., p. 149 (Fifth Edition, Lea & Febiger, Philadelphia, Pa. 1953).
2. Merck Manual: Lyght, C. E., p. 1102 (Ninth Edition, Merck & Co., Inc., Rahway, N. J. 1956).

relieves both muscle spasm and joint inflammation

MSD MERCK SHARP & DOHME Philadelphia 1, Pa.
Division of MERCK & CO., INC.

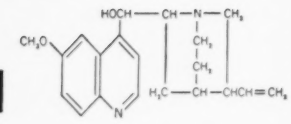
Progress in SYNTHETIC CHEMISTRY EQUALS *Progress in* CHEMOTHERAPEUTICS

"It has a high degree of clinical safety. . . It is considered to be the preferred antimalarial drug for treatment of disorders of connective tissue, because of the low incidence of gastrointestinal distress as compared to that with chloroquine phosphate."[1]

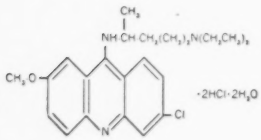
"... Plaquenil is decidedly less toxic and better tolerated by the average patient, even in high dosage, than is chloroquine."[2]

"... the least toxic of its class ..."[3]

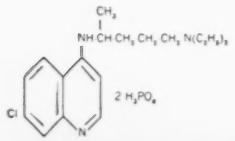
QUININE



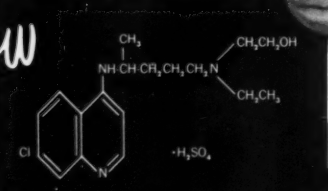
ATABRINE® HYDROCHLORIDE



ARALEN® PHOSPHATE



Now



Plaquenil® SULFATE

Remarkably effective in RHEUMATOID ARTHRITIS

SIDE EFFECTS MARKEDLY REDUCED

DOSE: Initial – 400 to 600 mg. (2 or 3 tablets) Plaquenil sulfate daily.
Maintenance – 200 to 400 mg. (1 or 2 tablets) daily.

SUPPLIED: Tablets of 200 mg., bottles of 100.

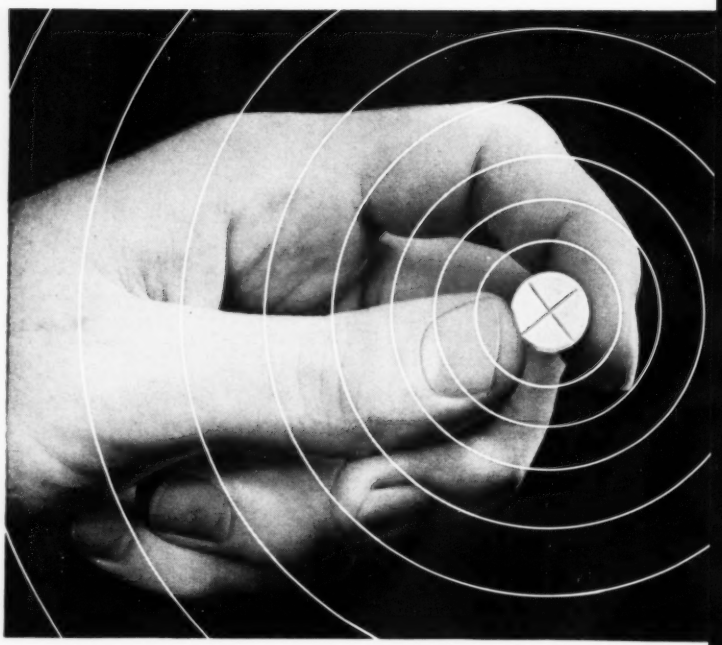
Write for Booklet

Winthrop LABORATORIES NEW YORK 18, N. Y.

REFERENCES:

1. Scherbel, A.L., Schuchter, S.L., and Harrison, J.W.: *Cleveland Clin. Quart.* 24:98, Apr., 1957.
2. Schoch, A.G., and Alexander, L.J.: The Schoch section, *Bull. A. Mil. Dermatologists* 5:25, Nov., 1956.
3. Cornbleet, Theodore: Arch. Dermat. 73:572, June, 1956.

ONLY
ONE
TABLET
A
DAY



now... unprecedented Sulfa therapy

KYNEX*

SULFAMETHOXYPYRIDAZINE LEDERLE

New authoritative studies show that KYNEX dosage can be reduced even further than that recommended earlier.[1] Now, clinical evidence has established that a single (0.5 Gm.) tablet maintains therapeutic blood levels extending beyond 24 hours. Still more proof that KYNEX stands alone in sulfa performance—

- Lowest Oral Dose In Sulfa History—0.5 Gm. (1 tablet) daily in the usual patient for maintenance of therapeutic blood levels
- Higher Solubility—effective blood concentrations within an hour or two
- Effective Antibacterial Range—exceptional effectiveness in urinary tract infections
- Convenience—the low dose of 0.5 Gm. (1 tablet) per day offers optimum convenience and acceptance to patients

NEW DOSAGE

The recommended adult dose is 1 Gm. (2 tablets or 4 teaspoonfuls of syrup) the first day, followed by 0.5 Gm. (1 tablet or 2 teaspoonfuls of syrup) every day thereafter, or 1 Gm. every other day for mild to moderate infections. In severe infections where prompt, high blood levels are indicated, the initial dose should be 2 Gm. followed by 0.5 Gm. every 24 hours. Dosage in children, according to weight; i.e., a 40 lb. child should receive ¼ of the adult dosage. It is recommended that these dosages not be exceeded.

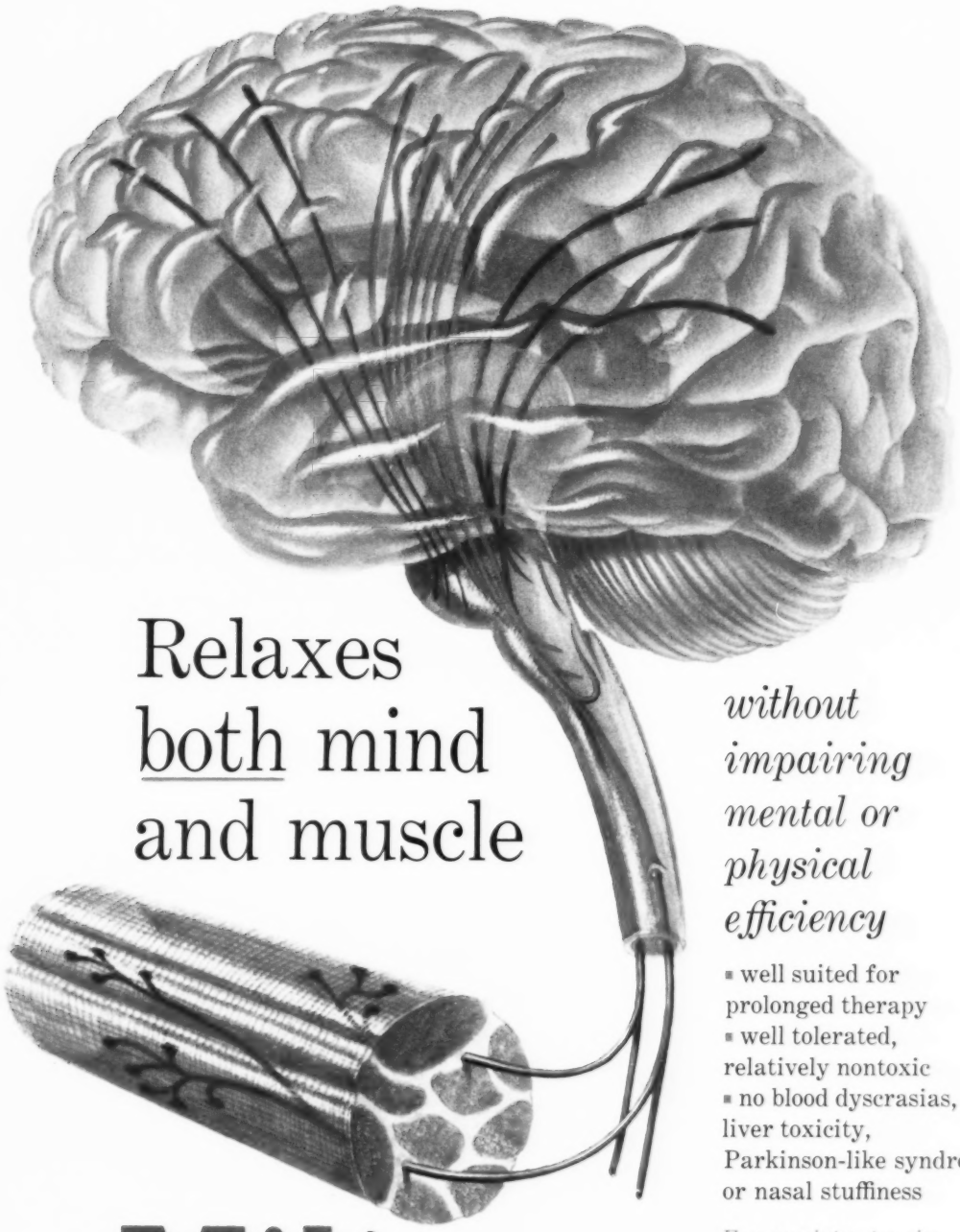
Tablets:
Each tablet contains 0.5 Gm. (7½ grains) of sulfamethoxypyridazine. Bottles of 24 and 100 tablets.

Syrup:
Each teaspoonful (5 cc.) of caramel-flavored syrup contains 250 mg. of sulfamethoxypyridazine. Bottle of 4 fl. oz.

[1] Nichols, R. L. and Finland, M.: J. Clin. Med. 49:410, 1957.

LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY, PEARL RIVER, NEW YORK

*Reg. U.S. Pat. Off.



Relaxes both mind and muscle

without impairing mental or physical efficiency

- well suited for prolonged therapy
- well tolerated, relatively nontoxic
- no blood dyscrasias, liver toxicity, Parkinson-like syndrome or nasal stuffiness

For anxiety, tension and muscle spasm in everyday practice.

Miltown®

2-methyl-2-**n**-propyl-1,3-propanediol dicarbamate

TRANQUILIZER WITH MUSCLE-RELAXANT ACTION

THE ORIGINAL MEPROBAMATE
DISCOVERED & INTRODUCED BY
WALLACE LABORATORIES
NEW BRUNSWICK, NEW JERSEY

Supplied:
400 mg. scored tablets,
200 mg. sugar-coated tablets.
Usual dosage:
One or two
400 mg. tablets t.i.d.

CM-6590

AN IMPORTANT ADVANCE IN MENOPAUSAL THERAPY

Because it replaces *half* control with *full* control.

Because it treats the *whole* menopausal syndrome.

Because *one* prescription manages *both* the psychic and somatic symptoms.

SUPPLIED: Bottles of 60 tablets.
Each tablet contains:

MILTOWN® (meprobamate, Wallace) ..... **400 mg.**
2-methyl-2-*n*-propyl-1,3-propanediol dicarbamate.

Conjugated Estrogens (equine) ..... **0.4 mg.**

DOSAGE: One tablet t.i.d. in 21-day courses with one week rest periods. Should be adjusted to individual requirements.

Samples and literature on request.

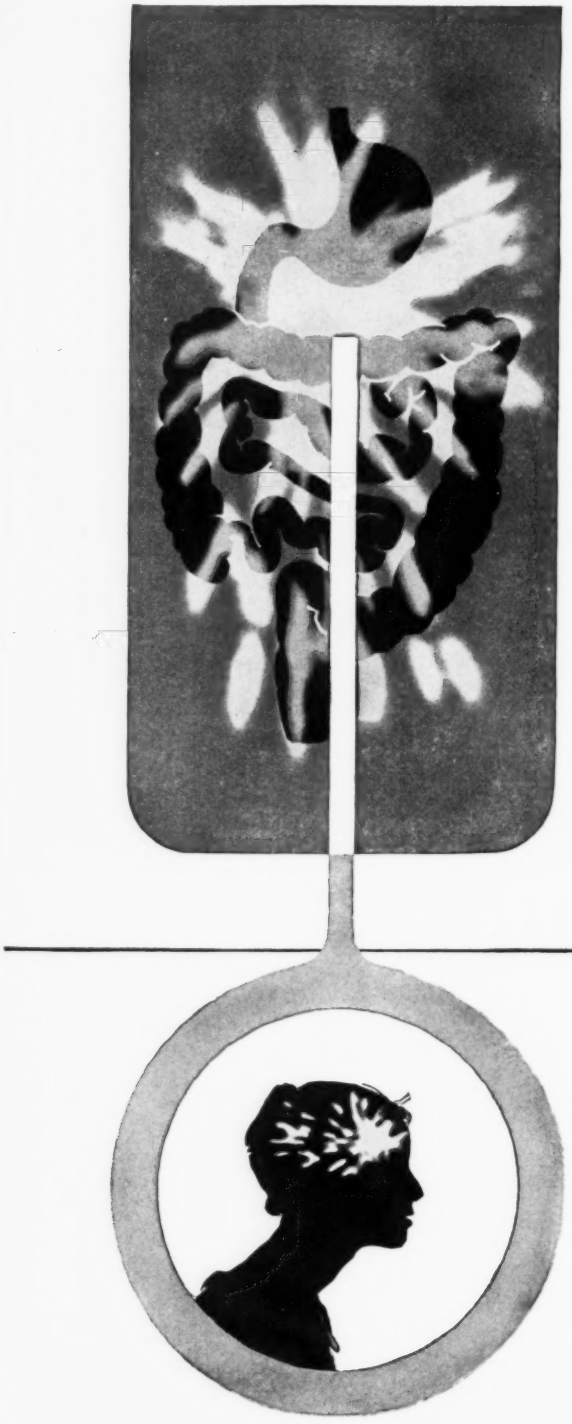
Two-dimensional treatment of the menopause

Milprem*

MILTOWN®
A Proven Tranquilizer + CONJUGATED ESTROGENS (EQUINE)
A Proven Estrogen

WALLACE LABORATORIES, *New Brunswick, N. J.*
who discovered and introduced Miltown, the original meprobamate.

*TRADE-MARK



in G.I. disorders

'Compazine' controls tension —often brings complete relief

In such conditions as gastritis, pylorospasm, peptic ulcer and spastic colitis, 'Compazine' not only relieves anxiety and tension, but also controls the nausea and vomiting which often complicate these disorders.

Physicians who have used 'Compazine' in gastrointestinal disorders —often in chronic, unresponsive cases—have had gratifying results (87% favorable).

*Compazine**

the tranquilizer and antiemetic remarkable for its freedom from drowsiness and depressing effect

Available: Tablets, Ampuls, Multiple dose vials, Spansule® sustained release capsules, Syrup and Suppositories.

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